=> d his

```
(FILE 'HOME' ENTERED AT 11:26:38 ON 07 JUL 2005)
                SET COST OFF
     FILE 'HCAPLUS' ENTERED AT 11:26:44 ON 07 JUL 2005
                E EPH
              4 S E3()A2
L1
L2
            154 S E29, E32
            156 S L1, L2
L3
                E KIENER P/AU
             99 S E3, E4, E7, E8
L4
                E KINCH M/AU
             66 S E3,E5,E7,E10,E11
L5
                E LANGERMAN S/AU
L6
             37 S E4,E5,E11-E14
                E MEDIMMUN/PA,CS
L7
            218 S MEDIMMUNE?/PA,CS
L8
              1 S US20050049176/PN OR (US2004-823259# OR WO2004-US11481 OR US20
L9
              1 S L3 AND L8
L10
            106 S L3 AND (PD<=20030411 OR PRD<=20030411 OR AD<=20030411)
L11
             59 S EPHRIN TYPE A RECEPTOR 2
L12
             27 S L11 AND (PD<=20030411 OR PRD<=20030411 OR AD<=20030411)
L13
            117 S L10, L12
     FILE 'REGISTRY' ENTERED AT 11:33:54 ON 07 JUL 2005
                E EPH/CN
                E EPHA2
L14
             27 S E3
L15
              0 S EPH A2
     FILE 'HCAPLUS' ENTERED AT 11:36:36 ON 07 JUL 2005
L16
            130 S L14
L17
             25 S ECK() (KINASE OR RECEPTOR KINASE OR RECEPTOR PROTEIN KINASE OR
L18
             1 S EPITHELIAL CELL RECEPTOR PROTEIN TYROSINE KINASE
            117 S L16-L18 AND (PD<=20030411 OR PRD<=20030411 OR AD<=20030411)
L19
L20
            174 S L13, L19
L21
             29 S L4-L7 AND L20
L22
             29 S L21 AND (?KINASE? OR TYROSINE OR PROTEINKINASE OR PROTEIN KIN
L23
             28 S L22 AND RECEPTOR
L24
             29 S L22, L23
L25
            29 S L9,L24
L26
            14 S L4-L7 AND L3,L11,L16-L18 NOT L25
L27
           193 S L3,L11,L16-L18 NOT L25,L26
L28
            145 S L27 AND L10, L12, L19
L29
             9 S L28 AND ANTAGON?
L30
             61 S L28 AND (INHIBIT? OR BLOCK? OR PREVENT?)
L31
             62 S L29, L30
                SEL DN AN 3 6 14-16 20 30 34 39 47 48 50 52 53 60
L32
             15 S L31 AND E1-E45
L33
             44 S L25, L32
             83 S L28 NOT L31, L25, L26
L34
                SEL DN AN 4 5 8 26 27 32 34 38 41 68 83
L35
             11 S L34 AND E46-E78
L36
             55 S L33, L35 AND L1-L13, L16-L35
L37
             55 S L36 AND (?TYROSIN? OR ?KINASE? OR RECEPTOR OR PROTEIN)
L38
             10 S L37 AND ECK
L39
             51 S L37 AND (EPH OR EPHRIN? OR EPH## OR EPH A#)
L40
             55 S L37-L39
```

SEL HIT RN

```
FILE 'REGISTRY' ENTERED AT 12:19:56 ON 07 JUL 2005
L41
             2 S E79-E80
L42
             2 S L41 AND L14
=> fil reg
FILE 'REGISTRY' ENTERED AT 12:20:37 ON 07 JUL 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)
Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.
STRUCTURE FILE UPDATES:
                          6 JUL 2005 HIGHEST RN 853990-77-9
DICTIONARY FILE UPDATES:
                          6 JUL 2005 HIGHEST RN 853990-77-9
New CAS Information Use Policies, enter HELP USAGETERMS for details.
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005
  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.
*******************
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,
* effective March 20, 2005. A new display format, IDERL, is now
* available and contains the CA role and document type information. *
*******************
Crossover limits have been increased. See HELP CROSSOVER for details.
Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html
=> d ide can tot 142
L42 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN
    389189-17-7 REGISTRY
ED
    Entered STN: 04 Feb 2002
CN
    DNA (human HeLa cell gene ECK protein kinase cDNA plus flanks) (9CI)
    INDEX NAME)
OTHER NAMES:
CN
    1171: PN: WO03042661 TABLE: 34A claimed DNA
CN
    11: PN: WO02072789 PAGE: 120 unclaimed DNA
CN
    1259: PN: WO03095618 TABLE: 1 unclaimed DNA
CN
    1728: PN: WO03042661 TABLE: 3A claimed DNA
CN
    1: PN: WO03061564 TABLE: 1 unclaimed DNA
CN
    201: PN: WO0224956 FIGURE: 11 claimed DNA
CN
    219: PN: WO02059367 TABLE: 3 unclaimed DNA
    2257: PN: WO03042661 TABLE: 25A claimed DNA
CN
```

2381: PN: WO03042661 TABLE: 49A claimed DNA

25: PN: WO03044166 TABLE: 1 unclaimed DNA

2455: PN: WO2004038376 TABLE: 5 unclaimed DNA

256: PN: WO02072828 TABLE: 3 claimed sequence

CN CN

CN

CN

```
CN
     3428: PN: WO03042661 TABLE: 17A claimed DNA
CN
     34: PN: US20030233196 FIGURE: 2 unclaimed DNA
CN
     4034: PN: WO03091391 TABLE: 20 unclaimed DNA
CN
     4109: PN: WO2004037996 TABLE: 3 claimed DNA
CN
     7: PN: WO02063037 TABLE: 1 unclaimed DNA
     DNA (human cell line HeLa and keratinocyte cDNA)
CN
     DNA (human cell line HeLa and keratinocyte gene ECK cDNA)
CN
CN
     DNA (human keratinocyte gene EphA2 protein kinase cDNA plus
     flanks)
CN
     GenBank M36395 (Secondary GenBank Accession Number)
CN
     GenBank M59371
     NUCLEIC ACID SEQUENCE
FS
MF
     Unspecified
CI
     MAN
SR
     GenBank
LC
     STN Files:
                  CA, CAPLUS, GENBANK, TOXCENTER, USPATFULL
**RELATED SEQUENCES AVAILABLE WITH SEOLINK**
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
              20 REFERENCES IN FILE CA (1907 TO DATE)
              20 REFERENCES IN FILE CAPLUS (1907 TO DATE)
REFERENCE
            1: 140:402911
REFERENCE
            2:
                140:373461
REFERENCE
                140:37033
            3:
REFERENCE
                140:3792
            4:
REFERENCE
            5:
                139:379453
REFERENCE
            6:
                139:145007
REFERENCE
                139:18834
            7:
REFERENCE
            8:
                139:2019
REFERENCE
                139:2018
            9:
REFERENCE 10: 138:397234
L42 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN
     149433-91-0 REGISTRY
ED
     Entered STN: 20 Aug 1993
CN
     Kinase (phosphorylating), gene eck protein (9CI) (CA INDEX NAME)
OTHER NAMES:
     Eck kinase
CN
     Eck receptor kinase
CN
CN
     ECK receptor protein-tyrosine kinase
CN
     EphA2 receptor tyrosine kinase
CN
     Ephrin-A2 receptor tyrosine kinase
     Epithelial cell receptor protein tyrosine kinase
CN
CN
     Gene eck protein kinase
CN
     Gene eck receptor protein tyrosine kinase
CN
     Gene eck receptor tyrosine kinase
     Unspecified
MF
CI
     MAN
```

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

100 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

101 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:7711

REFERENCE 2: 142:460961

REFERENCE 3: 142:426447

REFERENCE 4: 142:254576

REFERENCE 5: 141:374716

REFERENCE 6: 141:273622

REFERENCE 7: 141:241427

REFERENCE 8: 141:150541

REFERENCE 9: 141:137529

REFERENCE 10: 141:121430

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 12:20:44 ON 07 JUL 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 7 Jul 2005 VOL 143 ISS 2 FILE LAST UPDATED: 6 Jul 2005 (20050706/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 140 all tot

L40 ANSWER 1 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:46212 HCAPLUS

DN 142:353435

ED Entered STN: 19 Jan 2005

```
ΤI
     Targeting tyrosine kinase in cancer
ΑU
     Dhawan, Deepika; Kinch, Michael S.; Knapp, Deborah W.
CS
     Veterinary Clinical Science, Lynn Hall of Veterinary Medicine, Purdue
     University, West Lafayette, IN, 47907-2026, USA
SO
     Recent Advances in Life Sciences (2002), 57-67. Editor(s):
     Bhattacharyya, Nandan; Bhattacharyya, Chandan. Publisher: Research
     Signpost, Trivandrum, India.
     CODEN: 69GJFV; ISBN: 81-7736-230-5
DT
     Conference; General Review
LA
     English
CC
     15-0 (Immunochemistry)
     Section cross-reference(s): 1, 7, 14
AB
     A review with refs. Receptor tyrosine kinases
     (RTKs) play an important role in signal transduction. One member of the
     Eph family, EphA2, a protein tyrosine
     kinase, is upregulated in aggressive and metastatic cancers.
     discuss here, the role of RTKs and the Eph family in particular,
     and the potential role of EphA2 as a target for cancer therapy.
     Monoclonal antibodies have been raised against EphA2. We
     present some of the recent findings involving the use of these antibodies
     as potential anti-cancer agents.
ST
     review receptor tyrosine kinase
     EphA2 monoclonal antibody antitumor cancer; metastatic cancer
     anticancer EphA2 therapeutic target monoclonal antibody review
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor
        2; targeting tyrosine kinase in cancer)
IT
     Neoplasm
        (metastasis; targeting tyrosine kinase in cancer)
IT
     Antibodies and Immunoglobulins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (monoclonal, against EphA2; targeting tyrosine
        kinase in cancer)
IT
     Antitumor agents
     Drug targets
     Neoplasm
     Signal transduction, biological
        (targeting tyrosine kinase in cancer)
TT
     340830-03-7
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (targeting tyrosine kinase in cancer)
              THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
(1) Adams, R; Genes Dev 1999, V13, P295 HCAPLUS
(2) Adams, R; Genes Dev 1999, V13, P295 HCAPLUS
(3) Andres, A; Oncogene 1994, V9, P1461 HCAPLUS
(4) Augustin, H; Cell Tissue Res 2003, V314, P25 HCAPLUS
(5) Berclaz, G; Ann Oncol 2003, V14, P220 MEDLINE
(6) Berclaz, G; Oncol Rep 2002, V9, P985 HCAPLUS
(7) Binns, K; Mol Cell Biol 2000, V20, P4791 HCAPLUS
(8) Bissell, M; Am J Pathol 1999, V155, P675 MEDLINE
(9) Brantley, D; Oncogene 2002, V21, P7011 HCAPLUS
(10) Bruckner, K; Curr Opin Neurobiol 1998, V8, P375 HCAPLUS
(11) Bruckner, K; Science 1997, V275, P1640 MEDLINE
(12) Carles-Kinch, K; Cancer Res 2002, V62, P2840 HCAPLUS
(13) Cheng, N; Cytokine Growth Factor Rev 2002, V13, P75 HCAPLUS
(14) Cheng, N; Neoplasia 2003, V5, P445 HCAPLUS
(15) Clarkson, R; Mol Endocrinol 1999, V13, P619 HCAPLUS
```

- (16) Coffman, K; Cancer Res 2003, V63, P7907 HCAPLUS
 (17) Connor, R; Dev Biol 1998, V193, P21 HCAPLUS
 (18) Daniel, T; Kidney Int Suppl 1996, V57, PS73 HCAPLUS
- (19) Davis, S; Science 1994, V266, P816 HCAPLUS
- (20) Davy, A; Embo J 2000, V19, P5396 HCAPLUS
- (21) Davy, A; Genes Dev 1999, V13, P3125 HCAPLUS
- (22) Dodelet, V; J Biol Chem 1999, V274, P31941 HCAPLUS
- (23) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS
- (24) Dohn, M; Oncogene 2001, V20, P6503 HCAPLUS
- (25) Easty, D; Melanoma Res 2000, V10, P401 HCAPLUS
- (26) Flanagan, J; Annu Rev Neurosci 1998, V21, P309 HCAPLUS
- (27) Gerety, S; Mol Cell 1999, V4, P403 HCAPLUS
- (28) Gu, C; Mol Cell Biol 2001, V21, P4579 HCAPLUS
- (29) Hafner, C; Int J Oncol 2003, V23, P1553 HCAPLUS
- (30) Henkemeyer, M; Cell 1996, V86, P35 HCAPLUS
- (31) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS
- (32) Himanen, J; Int J Biochem Cell Biol 2003, V35, P130 HCAPLUS
- (33) Himanen, J; Int J Biochem Cell Biol 2003, V35, P130 HCAPLUS
- (34) Himanen, J; Nature 1998, V396, P486 HCAPLUS
- (35) Hock, B; Proc Natl Acad Sci U S A 1998, V95, P9779 HCAPLUS
- (36) Holland, S; Nature 1996, V383, P722 HCAPLUS
- (37) Huai, J; J Biol Chem 2001, V276, P6689 HCAPLUS
- (38) Kalo, M; Biochemistry 1999, V38, P14396 HCAPLUS
- (39) Kikawa, K; J Biol Chem 2002, V277, P39274 HCAPLUS
- (40) Kinch, M; Clin Cancer Res 2003, V9, P613 HCAPLUS
- (41) Konopka, G; Curr Mol Med 2003, V3, P73 HCAPLUS
- (42) Kullander, K; Neuron 2001, V29, P73 HCAPLUS
- (43) Lin, T; J Cell Biol 1997, V136, P1385 HCAPLUS
- (44) Liu, W; Cancer 2002, V94, P934 HCAPLUS
- (45) Lu, M; Cancer Res 2003, V63, P3425 HCAPLUS
- (46) Luo, H; J Immunol 2001, V167, P1362 HCAPLUS
- (47) Maniotis, A; Am J Pathol 1999, V155, P739 MEDLINE
- (48) Maulik, G; Methods Mol Med 2003, V74, P113 HCAPLUS
- (49) McBride, J; Mech Dev 1998, V77, P201 HCAPLUS
- (50) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
- (51) Miyazaki, T; Int J Cancer 2003, V103, P657 HCAPLUS
- (52) Munaron, L; Int J Mol Med 2002, V10, P671 HCAPLUS
- (53) Myers, C; J Cell Biol 2000, V148, P343 HCAPLUS
- (54) Nakamoto, M; Microsc Res Tech 2002, V59, P58 HCAPLUS
- (55) Nemoto, T; Pathobiology 1997, V65, P195 HCAPLUS
- (56) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
- (57) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS
- (58) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS
- (59) Pandey, A; Science 1995, V268, P567 HCAPLUS
- (60) Pawson, T; Eur J Cancer 2002, V38, PS3
- (61) Pawson, T; Science 1997, V278, P2075 HCAPLUS
- (62) Pratt, R; Oncogene 2002, V21, P7690 HCAPLUS
- (63) Rogers, J; Mech Dev 1999, V87, P119 HCAPLUS
- (64) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
- (65) Sawai, Y; J Hepatol 2003, V39, P991 HCAPLUS
- (66) Shimoyama, M; Biochem Biophys Res Commun 2002, V298, P87 HCAPLUS
- (67) Stapleton, D; Nat Struct Biol 1999, V6, P44 HCAPLUS
- (68) Stephenson, S; B M C Mol Biol 2001, V2, P15 MEDLINE
- (69) Sullivan, D; Br J Cancer 2003, V89, P228 HCAPLUS
- (70) Takai, N; Oncol Rep 2001, V8, P567 HCAPLUS
- (71) Tang, X; Clin Cancer Res 1999, V5, P1491 HCAPLUS
- (72) Tang, X; Clin Cancer Res 1999, V5, P455 HCAPLUS
- (73) Tang, X; Med Pediatr Oncol 2000, V35, P656 MEDLINE
- (74) Tang, X; Med Pediatr Oncol 2001, V36, P80 MEDLINE
- (75) Tang, X; Proc Natl Acad Sci U S A 2000, V97, P10936 HCAPLUS

```
(76) Tuzi, N; Br J Cancer 1994, V69, P417 HCAPLUS
(77) Vanhoutte, P; J Biol Chem 2001, V276, P5189 HCAPLUS
(78) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
(79) Wang, H; Cell 1998, V93, P741 HCAPLUS
(80) Wang, Y; Biochem Biophys Res Commun 2002, V296, P214 HCAPLUS
(81) Wilkinson, D; Int Rev Cytol 2000, V196, P177 HCAPLUS
(82) Yu, J; Proc Natl Acad Sci U S A 1999, V96, P14517 HCAPLUS
(83) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
(84) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
(85) Zeng, G; Am J Pathol 2003, V163, P2271 HCAPLUS
(86) Zisch, A; Oncogene 2000, V19, P177 HCAPLUS
L40
    ANSWER 2 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2004:905876 HCAPLUS
DN
     141:360679
ED
     Entered STN: 29 Oct 2004
     EphA2, hypoproliferative cell disorders and epithelial and
TI
     endothelial reconstitution
IN
     Kiener, Peter A.; Kinch, Michael S.; Langermann,
     Solomon
     Medimmune, Inc., USA
PA
     PCT Int. Appl., 82 pp.
so
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
     ICM C12N
TC
     1-7 (Pharmacology)
CC
     Section cross-reference(s): 3, 6, 13
FAN.CNT 1
     PATENT NO.
                        KIND
                                       APPLICATION NO.
                               DATE
     -----
                               -----
                                          -----
                        ----
                               20041028 WO 2004-US11481
PΙ
     WO 2004092343
                        A2
                                                               20040412 <--
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
            BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
            ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
            SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
            TD, TG
     US 2005049176
                               20050303
                                        US 2004-823259
                         A1
                                                                 20040412 <--
PRAI US 2003-462009P
                         Ρ
                               20030411 <--
                CLASS PATENT FAMILY CLASSIFICATION CODES
               ----
WO 2004092343
                ICM
                       C12N
US 2005049176 NCL
                       514/002.000; 514/044.000
     The present invention relates to methods and compns. designed for the
     treatment, management, or prevention of a hypoproliferative cell disorder,
     especially those disorders relating to the destruction, shedding, or inadequate
     proliferation of epithelial and/or endothelial cells, particularly
     interstitial cystitis (IC) and lesions associated with inflammatory bowel
     disease (IBD). The methods of the invention comprise the administration
     of an effective amount of one or more agents that are antagonists of
     EphA2. In certain embodiments, the EphA2 antagonistic
     agent of the invention decreases EphA2endogenous ligand binding,
     upregulates EphA2 gene expression and/or translation, increases
```

ST

IT

TΤ

ΙT

IT

TT

TT

IT

IT

IT

IT

```
EphA2 protein stability or protein
accumulation, decreases EphA2 cytoplasmic tail phosphorylation,
promotes EphA2 kinase activity (other than
autophosphorylation or ligand mediated EphA2 signaling),
increases proliferation of EphA2 expressing cells, increases
survival of EphA2 expressing cells, and/or
maintains/reconstitutes epithelial and/or endothelial cell layer
integrity. The invention also provides pharmaceutical compns. comprising
one or more EphA2 antagonistic agents of the invention either
alone or in combination with one or more other agents useful for therapy
for a hypoproliferative cell disorder. Diagnostic methods and methods for
screening for therapeutically useful agents are also provided.
EphA2 hypoproliferative cell disorder epithelium endothelium
reconstitution
Antigens
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);
ANST (Analytical study); BIOL (Biological study); USES (Uses)
   (EphA2; ephA2, hypoproliferative cell disorders and
   epithelial and endothelial reconstitution)
Bladder, disease
Inflammation
   (cystitis, interstitial; ephA2, hypoproliferative cell
   disorders and epithelial and endothelial reconstitution)
Cell death
Human
Immunomodulators
   (ephA2, hypoproliferative cell disorders and epithelial and
   endothelial reconstitution)
Antisense nucleic acids
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL
(Biological study); PREP (Preparation); USES (Uses)
   (ephA2, hypoproliferative cell disorders and epithelial and
   endothelial reconstitution)
Proteins
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL
(Biological study); PREP (Preparation); USES (Uses)
   (ephrin A2; ephA2, hypoproliferative cell disorders
   and epithelial and endothelial reconstitution)
Tyrosine kinase receptors
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL
(Biological study); PREP (Preparation); USES (Uses)
   (ephrin type-A receptor
   2; ephA2, hypoproliferative cell disorders and
   epithelial and endothelial reconstitution)
Proteins
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL
(Biological study); PREP (Preparation); USES (Uses)
   (ephrin, A1; ephA2, hypoproliferative cell
   disorders and epithelial and endothelial reconstitution)
Cell proliferation
   (epithelial; ephA2, hypoproliferative cell disorders and
   epithelial and endothelial reconstitution)
Antibodies and Immunoglobulins
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); ANST
(Analytical study); BIOL (Biological study); PREP (Preparation); USES
(Uses)
   (humanized, to EphA2; ephA2, hypoproliferative cell
   disorders and epithelial and endothelial reconstitution)
Urinary tract, disease
   (infection, treatment of; ephA2, hypoproliferative cell
```

```
disorders and epithelial and endothelial reconstitution)
TT
     Intestine, disease
        (inflammatory, treatment of; ephA2, hypoproliferative cell
        disorders and epithelial and endothelial reconstitution)
IT
     Antibodies and Immunoglobulins
     RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); ANST
     (Analytical study); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (monoclonal, to EphA2; ephA2, hypoproliferative
        cell disorders and epithelial and endothelial reconstitution)
IT
     Endothelium
     Epithelium
        (proliferation; ephA2, hypoproliferative cell disorders and
        epithelial and endothelial reconstitution)
IT
     Disease, animal
        (proliferative, treatment of; ephA2, hypoproliferative cell
        disorders and epithelial and endothelial reconstitution)
IT
     Double stranded RNA
     RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (small interfering; ephA2, hypoproliferative cell disorders
        and epithelial and endothelial reconstitution)
IT
     Antibodies and Immunoglobulins
     RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);
     ANST (Analytical study); BIOL (Biological study); USES (Uses)
        (to EphA2; ephA2, hypoproliferative cell disorders
        and epithelial and endothelial reconstitution)
IT
     778187-38-5
                   778187-39-6
                                 778187-40-9
                                               778187-41-0
                                                            778187-42-1
     778187-43-2
     RL: PRP (Properties)
        (unclaimed nucleotide sequence; ephA2, hypoproliferative cell
        disorders and epithelial and endothelial reconstitution)
     778187-37-4
IT
     RL: PRP (Properties)
        (unclaimed protein sequence; ephA2,
        hypoproliferative cell disorders and epithelial and endothelial
        reconstitution)
     95088-49-6
                 113516-56-6
                                113846-65-4
                                              113846-66-5
                                                             122024-47-9
IT
     130838-28-7
                   132328-28-0
                                 135702-75-9
                                               137235-69-9
                                                             154511-01-0
                   154511-04-3
     154511-02-1
                                 154511-05-4
                                               154511-06-5
                                                              154511-07-6
     154511-08-7
                   154511-09-8
                                 154511-10-1
                                               154511-11-2
                                                              154511-12-3
     154561-14-5
                   160918-30-9
                                 174490-42-7
                                               185047-03-4
                                                              200405-35-2
     206748-57-4
                   244250-73-5
                                 244283-56-5
                                               261944-63-2
                                                              278595-84-9
                                 447456-94-2
     285552-09-2
                   337489-94-8
                                               447456-95-3
                                                              455901-21-0
     455901-22-1
                   455901-23-2
     RL: PRP (Properties)
        (unclaimed sequence; ephA2, hypoproliferative cell disorders
        and epithelial and endothelial reconstitution)
L40
    ANSWER 3 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2004:902103 HCAPLUS
DN
     141:394078
ED
     Entered STN: 28 Oct 2004
TT
     Recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of
     autoimmune diseases, inflammatory diseases, proliferative diseases and
     infections
IN
     Reed, Jennifer L.
PA
    Medimmune, Inc., USA
SO
     PCT Int. Appl., 291 pp.
     CODEN: PIXXD2
```

```
DT
    Patent
LA
    English
IC
    ICM A61K
CC
     15-3 (Immunochemistry)
     Section cross-reference(s): 1, 3, 9, 63
FAN.CNT 1
    PATENT NO.
                        KIND
                               DATE
                                        APPLICATION NO.
     -----
                        ----
                               -----
                                          -----
    WO 2004091510
PΙ
                               20041028 WO 2004-US11172 20040412 <--
                        A2
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
            BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
            ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
            SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
            TD, TG
    US 2005002934
                         A1
                               20050106
                                        US 2004-823253
                                                                 20040412 <--
                         P
PRAI US 2003-462259P
                               20030411 <--
                         P
    US 2003-477797P
                               20030610
CLASS
 PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
 -----
WO 2004091510 ICM
                       A61K
WO 2004091510 ECLA
                       C07K016/24F
                                                                         <--
US 2005002934 NCL
                       424/145.100; 530/388.230; 435/007.100
    The present invention provides novel antibodies that immunospecifically
    bind to an IL-9 polypeptide and compns. comprising said antibodies. The
    antibodies are anti-human IL-9 antibody 4D4, 4D4H2-1D11, 4D4com-XF9,
    4D4com-2F9, 7F3, 71A10, 22D3, 7F3com-2H2, 7F3com-3H5 and 7F3com-3D4.
    present invention also provides methods and compns. preventing, treating,
    managing, and/or ameliorating diseases and disorders associated with aberrant
    expression and/or activity of IL-9 or IL-9 receptor or subunits
    thereof, autoimmune diseases, inflammatory diseases, proliferative
    diseases, and infections comprising administration of one or more
    antibodies thereof that immunospecifically bind to an IL-9 polypeptide.
    The invention also encompasses methods and compns. for diagnosing,
    monitoring, and prognosing these disorders. The present invention further
    relates to articles of manufacture and kits comprising antibodies that
    immunospecifically bind to an IL-9 polypeptide.
ST
    recombinant antibody human interleukin 9 autoimmune disease inflammation
    infection; proliferative disease asthma allergy monoclonal antibody human
    IL9 receptor
IT
    Antibodies and Immunoglobulins
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (IgG; recombinant anti-IL-9 antibodies for diagnosis, prognosis and
       treatment of autoimmune diseases, inflammatory diseases, proliferative
       diseases and infections)
IT
    Tumor necrosis factors
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
    (Biological study); USES (Uses)
        (antagonists; recombinant anti-IL-9 antibodies for diagnosis, prognosis
       and treatment of autoimmune diseases, inflammatory diseases,
       proliferative diseases and infections)
IT
    Mycosis
```

(aspergillosis; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Infection

Pneumonia

(bacterial; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Samples

(biol.; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Mycosis

(candidiasis; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Drug delivery systems

(carriers; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Antibodies and Immunoglobulins

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(chimeric; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Lung, disease

(chronic obstructive; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Inflammation

(chronic; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Antibodies and Immunoglobulins

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (conjugates; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Physical properties

(consts., association; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Medical goods

(containers; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Mycosis

(cryptococcosis; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections)

IT Tyrosine kinase receptors

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ephrin type-A receptor

2, anti-; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections) IT

Lung, disease

```
(fibrosis; recombinant anti-IL-9 antibodies for diagnosis, prognosis
        and treatment of autoimmune diseases, inflammatory diseases,
        proliferative diseases and infections)
     Antibodies and Immunoglobulins
IT
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (fragments; recombinant anti-IL-9 antibodies for diagnosis, prognosis
        and treatment of autoimmune diseases, inflammatory diseases,
        proliferative diseases and infections)
ΙT
     Antibodies and Immunoglobulins
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (heavy chain; recombinant anti-IL-9 antibodies for diagnosis, prognosis
        and treatment of autoimmune diseases, inflammatory diseases,
        proliferative diseases and infections)
IT
     Antibodies and Immunoglobulins
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (humanized; recombinant anti-IL-9 antibodies for diagnosis, prognosis
        and treatment of autoimmune diseases, inflammatory diseases,
        proliferative diseases and infections)
IT
     Diagnosis
        (immunodiagnosis; recombinant anti-IL-9 antibodies for diagnosis,
        prognosis and treatment of autoimmune diseases, inflammatory diseases,
        proliferative diseases and infections)
IT
     Respiratory tract, disease
        (infection; recombinant anti-IL-9 antibodies for diagnosis, prognosis
        and treatment of autoimmune diseases, inflammatory diseases,
        proliferative diseases and infections)
IT
     Interleukin receptors
     RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (interleukin 9; recombinant anti-IL-9 antibodies for diagnosis,
        prognosis and treatment of autoimmune diseases, inflammatory diseases,
        proliferative diseases and infections)
     Antibodies and Immunoglobulins
IT
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (light chain; recombinant anti-IL-9 antibodies for diagnosis, prognosis
        and treatment of autoimmune diseases, inflammatory diseases,
        proliferative diseases and infections)
     Containers
IT
        (medical; recombinant anti-IL-9 antibodies for diagnosis, prognosis and
        treatment of autoimmune diseases, inflammatory diseases, proliferative
        diseases and infections)
    Mast cell
IT
        (modulator; recombinant anti-IL-9 antibodies for diagnosis, prognosis
        and treatment of autoimmune diseases, inflammatory diseases,
        proliferative diseases and infections)
IT
    Antibodies and Immunoglobulins
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (monoclonal; recombinant anti-IL-9 antibodies for diagnosis, prognosis
        and treatment of autoimmune diseases, inflammatory diseases,
```

proliferative diseases and infections) TΤ Drug delivery systems (nasal, intra-; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections) TT Drug delivery systems (oral; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections) IT Drug delivery systems (parenterals; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections) IT Packaging materials (pharmaceutical; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections) IT Disease, animal (proliferative; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections) Fibrosis IT (pulmonary; recombinant anti-IL-9 antibodies for diagnosis, prognosis and treatment of autoimmune diseases, inflammatory diseases, proliferative diseases and infections) IT Affinity Allergy Angiogenesis inhibitors Animal cell Animal tissue Anti-inflammatory agents Antibacterial agents Antitumor agents Antiviral agents Arthritis Asthma Autoimmune disease Combination chemotherapy DNA sequences Dissociation constant Drug delivery systems Drugs Fungicides Human Human metapneumovirus Human parainfluenza virus Immunomodulators Immunotherapy Infection Inflammation Labels Medical goods Molecular cloning Multiple sclerosis Mycosis Neoplasm Prognosis Protein sequences

Respiratory syncytial virus

Rheumatoid arthritis

```
Test kits
    Tuberculosis
        (recombinant anti-IL-9 antibodies for diagnosis, prognosis and
       treatment of autoimmune diseases, inflammatory diseases, proliferative
       diseases and infections)
TΤ
    Antibodies and Immunoglobulins
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL-
     (Biological study); PREP (Preparation); USES (Uses)
        (recombinant anti-IL-9 antibodies for diagnosis, prognosis and
       treatment of autoimmune diseases, inflammatory diseases, proliferative
       diseases and infections)
IT
     Interleukin 9
    RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (recombinant anti-IL-9 antibodies for diagnosis, prognosis and
       treatment of autoimmune diseases, inflammatory diseases, proliferative
       diseases and infections)
IT
     Infection
        (viral; recombinant anti-IL-9 antibodies for diagnosis, prognosis and
       treatment of autoimmune diseases, inflammatory diseases, proliferative
       diseases and infections)
ΙT
    784245-11-0P
                   784374-05-6P
                                   784374-06-7P
                                                  784374-07-8P
                                                                 784374-08-9P
    784374-09-0P
                   784374-10-3P
                                   784374-11-4P
                                                  784374-12-5P
                                                                 784374-13-6P
    784374-14-7P
                   784374-15-8P
                                   784374-16-9P
                                                  784374-17-0P
                                                                 784374-18-1P
    784374-19-2P
                   784374-20-5P
                                   784374-21-6P
                                                  784374-25-0P, Interleukin 9
              784374-26-1P
                             784374-27-2P
                                             784374-31-8P
                                                           784374-32-9P
    784374-33-0P, Interleukin 9 receptor (human)
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (amino acid sequence; recombinant anti-IL-9 antibodies for diagnosis,
       prognosis and treatment of autoimmune diseases, inflammatory diseases,
       proliferative diseases and infections)
IT
    784374-22-7P
                   784374-23-8P
                                   784374-24-9P
                                                  784374-28-3P, DNA (human
     interleukin 9 receptor cDNA)
                                    784374-29-4P
                                                   784374-30-7P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (nucleotide sequence; recombinant anti-IL-9 antibodies for diagnosis,
       prognosis and treatment of autoimmune diseases, inflammatory diseases,
       proliferative diseases and infections)
IT
                  480929-81-5, GenBank AAC17735
                                                   784200-47-1
                                                                 784200-48-2
    208518-20-1
    784200-49-3
                  784200-50-6
                                 784200-51-7
                                               784200-52-8
                                                             784200-53-9
    784200-54-0
                  784200-55-1
                                 784200-56-2
                                               784200-59-5
                                                             784200-60-8
    784200-61-9
    RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (recombinant anti-IL-9 antibodies for diagnosis, prognosis and
       treatment of autoimmune diseases, inflammatory diseases, proliferative
       diseases and infections)
IT
    188039-54-5, Palivizumab
                               288392-69-8, MEDI-507
                                                       324740-00-3, Vitaxin
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (recombinant anti-IL-9 antibodies for diagnosis, prognosis and
       treatment of autoimmune diseases, inflammatory diseases, proliferative
       diseases and infections)
ΙT
    246223-20-1
                  784374-42-1
                                 784374-43-2
                                               784374-44-3
                                                             784374-45-4
```

jan delaval - 7 july 2005

(unclaimed nucleotide sequence; recombinant anti-IL-9 antibodies for

784374-46-5

RL: PRP (Properties)

784374-47-6

```
diagnosis, prognosis and treatment of autoimmune diseases; inflammatory
        diseases, proliferative diseases and infections)
IT
     784374-41-0
     RL: PRP (Properties)
        (unclaimed protein sequence; recombinant anti-IL-9 antibodies
        for diagnosis, prognosis and treatment of autoimmune diseases,
        inflammatory diseases, proliferative diseases and infections)
IT
     145060-92-0 145060-93-1
                                145061-00-3
                                              158512-03-9
     728944-79-4
                  784200-57-3
                                784200-58-4
     RL: PRP (Properties)
        (unclaimed sequence; recombinant anti-IL-9 antibodies for diagnosis,
        prognosis and treatment of autoimmune diseases, inflammatory diseases,
        proliferative diseases and infections)
L40
     ANSWER 4 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
     2004:902071 HCAPLUS
AN
DN
     141:374716
ED
     Entered STN: 28 Oct 2004
TI
     Therapeutic use of tyrosine kinase receptor
     ephrin type-A receptor 2 (
     EphA2) for treating hypoproliferative cell disorders
IN
     Kiener, Peter A.; Kinch, Michael S.; Langermann,
     Solomon; Reed, Jennifer L.
PA
     Medimmune, Inc., USA
SO
     PCT Int. Appl., 128 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM A61B
CC
     1-7 (Pharmacology)
     Section cross-reference(s): 3, 6, 13
FAN.CNT 1
     PATENT NO.
                        KIND
                               DATE
                                         APPLICATION NO.
                                                                 DATE
     -----
                        _ _ _ _
                               -----
                                          -----
     WO 2004091375
ΡI
                        A2
                               20041028 WO 2004-US11482
                                                                20040412 <--
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
            BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
            ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
            SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
            TD, TG
     US 2005059592
                         Α1
                               20050317
                                         US 2004-823254
                                                                 20040412 <--
PRAI US 2003-462024P
                         P
                               20030411 <--
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
 -----
                ----
                       _______
                ICM
 WO 2004091375
                       A61B
 US 2005059592
               NCL
                       514/012.000; 424/144.100
     The present invention relates to methods and compns. designed for the
AB
     treatment, management, or prevention of a non-neoplastic
    hyperproliferative cell or excessive cell accumulation disorders,
    particularly those involving hyperproliferation of epithelial or
     endothelial cells. In one embodiment, the methods of the invention
     comprise the administration of an effective amount of one or more
     EphA2 agonistic agents that bind to EphA2 and increase
```

```
EphA2 cytoplasmic tail phosphorylation and/or increase
EphA2 autophosphorylation. in cells which EphA2 has been
agonized. In another embodiment, the methods of the invention comprise
the administration of an effective amount of one or more EDHA2
agonistic agents that bind to EphA2 and reduce EphA2
activity (other than autophosphorylation). In another embodiment, the
methods of the invention comprise administration of an effective amount of
one or more EphA2 agonistic agents that bind to EphA2
and decrease a pathol.-causing cell phenotype (e.g., a pathol.-causing
epithelial cell phenotype or a pathol.-causing endothelial cell
phenotype). In another embodiment, the methods of the invention comprise
the administration of an effective amount of one or more EphA2
agonistic agents that are EphA2 antibodies that bind to
EphA2 with a very low Koff rate. In prefer-red embodiments,
agents of the invention are monoclonal antibodies. The invention also
provides pharmaceutical compns. comprising one or more EphA2
agonistic agents of the invention either alone or in combination with one
or more other agents useful in therapy for non-neoplastic
hyperproliferative cell or excessive cell accumulation disorders.
EphA2 hypoproliferative disorder epithelium endothelium human
tyrosine kinase receptor
Antigens
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);
ANST (Analytical study); BIOL (Biological study); USES (Uses)
   (EphA2; therapeutic use of tyrosine kinase
   receptor ephrin type-A
   receptor 2 (EphA2) for treating
   hypoproliferative cell disorders)
Antiarteriosclerotics
   (antiatherosclerotics; therapeutic use of tyrosine
   kinase receptor ephrin type-
   A receptor 2 (EphA2) for treating
   hypoproliferative cell disorders)
Lung, disease
   (chronic obstructive, treatment of; therapeutic use of tyrosine
   kinase receptor ephrin type-
   A receptor 2 (EphA2) for treating
   hypoproliferative cell disorders)
Proteins
RL: BPN (Biosynthetic preparation); DGN (Diagnostic use); THU (Therapeutic
use); BIOL (Biological study); PREP (Preparation); USES (Uses)
   (ephrin A2; therapeutic use of tyrosine
   kinase receptor ephrin type-
   A receptor 2 (EphA2) for treating
   hypoproliferative cell disorders)
Tyrosine kinase receptors
RL: BPN (Biosynthetic preparation); DGN (Diagnostic use); THU (Therapeutic
use); BIOL (Biological study); PREP (Preparation); USES (Uses)
   (ephrin type-A receptor
   2; therapeutic use of tyrosine kinase
   receptor ephrin type-A
   receptor 2 (EphA2) for treating
   hypoproliferative cell disorders)
Proteins
RL: BPN (Biosynthetic preparation); DGN (Diagnostic use); THU (Therapeutic
use); BIOL (Biological study); PREP (Preparation); USES (Uses)
   (ephrin, Al; therapeutic use of tyrosine
   kinase receptor ephrin type-
   A receptor 2 (EphA2) for treating
   hypoproliferative cell disorders)
```

ST

IT

IT

IT

IT

IT

IT

```
IT
     Cell proliferation
        (epithelial; therapeutic use of tyrosine kinase
        receptor ephrin type-A
        receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
TT
     Disease, animal
        (fibroproliferative, treatment of; therapeutic use of tyrosine
        kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
ΙT
     Kidney, disease
     Liver, disease
     Lung, disease
        (fibrosis, treatment of; therapeutic use of tyrosine
        kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     Fibrosis
        (hepatic, treatment of; therapeutic use of tyrosine
        kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
ΙT
     Antibodies and Immunoglobulins
     RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); ANST
     (Analytical study); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (humanized, to EphA2; therapeutic use of tyrosine
        kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     Blood vessel, disease
        (hyperproliferative, treatment of; therapeutic use of tyrosine
        kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     Bronchi, disease
        (hyperresponsiveness, treatment of; therapeutic use of tyrosine
        kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     Inflammation
     Lung, disease
        (interstitial pneumonitis, usual, desquamative, treatment of;
        therapeutic use of tyrosine kinase receptor
        ephrin type-A receptor 2
        (EphA2) for treating hypoproliferative cell disorders)
IT
     Eye, disease
        (macula, degeneration, treatment of; therapeutic use of
        tyrosine kinase receptor ephrin
        type-A receptor 2 (EphA2
        ) for treating hypoproliferative cell disorders)
IT
    Diagnosis
        (mol.; therapeutic use of tyrosine kinase
        receptor ephrin type-A
        receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
    Antibodies and Immunoglobulins
     RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); ANST
     (Analytical study); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
```

```
(monoclonal, to EphA2; therapeutic use of tyrosine
       kinase receptor ephrin type-
       A receptor 2 (EphA2) for treating
       hypoproliferative cell disorders)
IT
    Endothelium
    Epithelium
        (proliferation; therapeutic use of tyrosine kinase
        receptor ephrin type-A
        receptor 2 (EphA2) for treating
       hypoproliferative cell disorders)
IT
    Disease, animal
        (proliferative, treatment of; therapeutic use of tyrosine
       kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
       hypoproliferative cell disorders)
IT
     Fibrosis
        (pulmonary, treatment of; therapeutic use of tyrosine
       kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
       hypoproliferative cell disorders)
IT
     Fibrosis
        (renal, treatment of; therapeutic use of tyrosine
       kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
       hypoproliferative cell disorders)
IT
     Artery, disease
        (restenosis, treatment of; therapeutic use of tyrosine
       kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     Double stranded RNA
     RL: BPN (Biosynthetic preparation); DGN (Diagnostic use); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (small interfering; therapeutic use of tyrosine
        kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     Antiasthmatics
     Antiviral agents
     Cell death
     Cell migration
     Extracellular matrix
     Gene therapy
     Human
     Immunomodulators
        (therapeutic use of tyrosine kinase
        receptor ephrin type-A
        receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     Fibronectins
     Mucins
     RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP
     (Preparation)
        (therapeutic use of tyrosine kinase
        receptor ephrin type-A
        receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     Antisense nucleic acids
     RL: BPN (Biosynthetic preparation); DGN (Diagnostic use); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
```

```
(therapeutic use of tyrosine kinase
        receptor ephrin type-A
        receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
TT
     Ribozymes
     RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
     USES (Uses)
        (therapeutic use of tyrosine kinase
        receptor ephrin type-A
        receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     Antibodies and Immunoglobulins
     RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);
     ANST (Analytical study); BIOL (Biological study); USES (Uses)
        (to EphA2; therapeutic use of tyrosine
        kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     Asbestosis
     Asthma
     Atherosclerosis
     Behcet's syndrome
     Fibrosis
     Psoriasis
     Rous sarcoma virus
     Seborrhea
        (treatment of; therapeutic use of tyrosine kinase
        receptor ephrin type-A
        receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
     141907-41-7P, Matrix metalloproteinase
IT
     RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP
     (Preparation)
        (therapeutic use of tyrosine kinase
        receptor ephrin type-A
        receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
ΙT
     149433-91-0P, EphA2 receptor tyrosine
     RL: BPN (Biosynthetic preparation); DGN (Diagnostic use); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (therapeutic use of tyrosine kinase
        receptor ephrin type-A
        receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
ΙT
     780827-75-0
                   780827-76-1
                                 780827-77-2
                                               780827-78-3
                                                              780827-79-4
     780827-80-7
     RL: PRP (Properties)
        (unclaimed nucleotide sequence; therapeutic use of tyrosine
        kinase receptor ephrin type-
        A receptor 2 (EphA2) for treating
        hypoproliferative cell disorders)
IT
     780827-74-9
                   780827-81-8
                                 780827-82-9
                                               780827-83-0
                                                              780827-84-1
    RL: PRP (Properties)
        (unclaimed protein sequence; therapeutic use of
        tyrosine kinase receptor ephrin
        type-A receptor 2 (EphA2
        ) for treating hypoproliferative cell disorders)
IT
    95088-49-6
                  113516-56-6
                                113846-65-4 113846-66-5
                                                             122024-47-9
     130838-28-7
                   132328-28-0
                                 135702-75-9
                                               137235-69-9
                                                            154511-01-0
```

```
154511-02-1
                  154511-04-3
                                154511-05-4
                                             154511-06-5
                                                          154511-07-6
     154511-08-7
                  154511-09-8
                               154511-10-1
                                             154511-11-2 154511-12-3
     154561-14-5 160918-30-9
                               174490-42-7
                                             185047-03-4 200405-35-2
     206748-57-4
                  244250-73-5
                               244283-56-5
                                           261944-63-2
                                                          278595-84-9
     285552-09-2 337489-94-8
                               447456-94-2
                                             447456-95-3
                                                          455901-21-0
     455901-22-1
                 455901-23-2
    RL: PRP (Properties)
        (unclaimed sequence; therapeutic use of tyrosine
       kinase receptor ephrin type-
       A receptor 2 (EphA2) for treating
       hypoproliferative cell disorders)
    ANSWER 5 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
L40
AN
    2004:681585 HCAPLUS
DN
    141:167766
    Entered STN: 20 Aug 2004
ED
TI
    Eph/ephrin mediated modulation of cell adhesion and
     tumor cell metastasis
    Lackmann, Martin; Wimmer-Kleikamp, Sabine; Scott, Andrew; Vearing,
IN
    Christopher; Boyd, Andrew
PA
    Ludwig Institute for Cancer Research, Australia; Monash University; The
    Council of the Queensland Institute of Medical Research; The University of
    Queensland
so
    PCT Int. Appl., 59 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    English
IC
    ICM A61K038-00
    ICS A61K038-17; A61K038-48; A61K038-45; A61K039-395
CC
     1-6 (Pharmacology)
FAN.CNT 1
    PATENT NO.
                      KIND DATE
                                      APPLICATION NO.
     ______
                        ----
                              -----
                                         -----
                              20040819 WO 2004-AU142
PΙ
    WO 2004069264
                        A1
                                                              20040209 <--
        W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
            BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
            CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
            ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
            IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KR, KZ, KZ, KZ, LC,
            LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
            MZ, MZ, NA, NI
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
            BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
            MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
            GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN,
            GQ, GW, ML, MR, NE, SN, TD, TG
PRAI AU 2003-900541
                        Α
                              20030207 <--
CLASS
 PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
               ----
 -----
WO 2004069264
                ICM
                      A61K038-00
                ICS
                      A61K038-17; A61K038-48; A61K038-45; A61K039-395
WO 2004069264
               ECLA
                     A61K038/17C; A61K038/19
                                                                         <--
AB
    Methods and compns. for modulating ephrin/Eph
    receptor-mediated cell adhesion and/or cell repulsion are
    provided, particularly in relation to preventing,
    inhibiting or delaying tumor cell metastasis through modulation of
    Eph receptor-ephrin binding interactions and
    subsequent Eph receptor signaling. Particular agents
    useful according to the invention are agents which interfere with a
```

```
ephrin-Eph receptor binding such as soluble
     ephrins and Eph receptors and antibodies
     directed to ephrins and Eph receptors,
     ephrin-cytotoxic drug conjugates which kill tumor cells,
     metalloprotease inhibitors and inhibitors of
     protein tyrosine phosphatase activity.
ST
     Eph ephrin cell adhesion tumor metastasis
     tyrosine phosphatase metalloprotease
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (Eph receptor; Eph/ephrin
        mediated modulation of cell adhesion and tumor cell metastasis)
IT
     Adhesion, biological
     Antitumor agents
     Human
     Leukemia
     Melanoma
     Neoplasm
     Signal transduction, biological
        (Eph/ephrin mediated modulation of cell adhesion
        and tumor cell metastasis)
IT
     Leukemia
        (acute pre-B-cell; Eph/ephrin mediated modulation
        of cell adhesion and tumor cell metastasis)
TT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin A5; Eph/ephrin mediated
        modulation of cell adhesion and tumor cell metastasis)
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin B2; Eph/ephrin mediated
        modulation of cell adhesion and tumor cell metastasis)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor
        2; Eph/ephrin mediated modulation of cell
        adhesion and tumor cell metastasis)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor 3; Eph/
        ephrin mediated modulation of cell adhesion and tumor cell
        metastasis)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor 4; Eph/
        ephrin mediated modulation of cell adhesion and tumor cell
        metastasis)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor 7; Eph/
        ephrin mediated modulation of cell adhesion and tumor cell
        metastasis)
     Tyrosine kinase receptors
IT
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor 8; Eph/
        ephrin mediated modulation of cell adhesion and tumor cell
       metastasis)
ΙT
    Proteins
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin; Eph/ephrin mediated modulation
```

```
of cell adhesion and tumor cell metastasis)
IT
     Melanoma
     Neoplasm
        (metastasis; Eph/ephrin mediated modulation of cell
        adhesion and tumor cell metastasis)
IT
     Angiogenesis
        (neovascularization; Eph/ephrin mediated modulation
        of cell adhesion and tumor cell metastasis)
IT
     37205-61-1, Proteinase inhibitor
                                        79747-53-8, Tyrosine
     phosphatase
                   81669-70-7, Metalloprotease
                                                145266-99-5, Metalloprotease
     inhibitor
                149433-92-1, Eph kinase
     193099-09-1, ADAM-10
                           301156-53-6, Tyrosine phosphatase SHP2
     352548-19-7, LMW-PTP
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (Eph/ephrin mediated modulation of cell adhesion
        and tumor cell metastasis)
IT
     113440-58-7, Calicheamicin
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (Eph/ephrin mediated modulation of cell adhesion
        and tumor cell metastasis)
L40
     ANSWER 6 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
ΑN
     2004:452978 HCAPLUS
DN
     141:2317
ED
     Entered STN: 04 Jun 2004
ΤI
     Algorithms for rational design and selection of functional and
     hyperfunctional siRNA for gene silencing
     Khvorova, Anastasia; Reynolds, Angela; Leake, Devin; Marshall, William;
IN
     Scaringe, Stephen
     Dharmacon, Inc., USA
PA
     PCT Int. Appl., 199 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM A61K
CC
     3-1 (Biochemical Genetics)
     Section cross-reference(s): 1
FAN.CNT 27
     PATENT NO.
                         KIND
                                DATE
                                           APPLICATION NO.
                                                                   DATE
     ------
                         ----
                                            -----
PΙ
     WO 2004045543
                                20040603
                                            WO 2003-US36787
                         A2
                                                                   20031114 <--
     WO 2004045543
                         Α3
                                20050421
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     WO 2004045543
                         A2
                                20040603
                                          WO 2003-XA36787
                                                                  20031114 <--
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
```

```
KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XB36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ; GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XC36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XD36787
                                                               20031114 <-
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XE36787
                                                               20031114 <--
       AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XF36787
                                                               20031114 <-
       AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
       LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
```

```
KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                        WO 2003-XG36787
                                                               20031114 <-
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XH36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XI36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XJ36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD,
                                    TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XK36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
```

```
KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                        WO 2003-XL36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XM36787
                                                               20031114 <-
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XN36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG.
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                                       WO 2003-X036787
                     A2
                           20040603
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
   RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD,
                                    TG
                           20040603
WO 2004045543
                     A2
                                       WO 2003-XP36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
```

```
KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XQ36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XR36787
                                                               20031114 <-
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XS36787
                                                               20031114 <---
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XT36787
                                                               20031114 <-
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XU36787
                                                               20031114 <-
       AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
```

```
KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XV36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XW36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XX36787
                                                               20031114 <-
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XY36787
                                                               20031114 <-
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
        KZ, MD, RU, TJ
   RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
        BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
        MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
        GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004045543
                     A2
                           20040603
                                       WO 2003-XZ36787
                                                               20031114 <--
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
        TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
```

```
KZ, MD, RU, TJ
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-426137P
                         P
                                20021114
    US 2003-502050P
                         Ρ
                                20030910
    WO 2003-US36787
                         Α
                                20031114
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
 ______
                ____
                       _____
WO 2004045543
                ICM
                       A61K
    Efficient sequence specific gene silencing is possible through the use of
     siRNA-mediated RNA interference (RNAi) technol. By selecting particular
     siRNAs by rational design, one can maximize the generation of an effective
    gene silencing reagent, as well as methods for silencing genes. Nine
     algorithms are provided for selecting siRNA for a target gene by measuring
     the functionality of sequences of 19-25 nucleotides in length that are
     substantially complementary to a stretch of nucleotides of the target
     sequence, wherein said functionality is dependent upon non-target specific
     criteria. In one method, rationally designed siRNA can be identified by
    maximizing one or more of the following criteria: (1) a low GC content,
    preferably between about 30-52%; (2) at least 2, preferably at least 3 A
    or U bases at positions 15-19 of the siRNA on the sense strand; (3) an A
    base at position 3, 14, and 19; (4) an U base at position 10; (5) a base
     other than C at position 19; (6) a base other than G at position 13; (7) a
    melting temperature (Tm), which refers to the character of the internal repeat
     that results in inter- or intramol. structures for one strand of the
     duplex, that is preferably not stable at >50°, more preferably not
     stable at >37°, even more preferably not stable at >30°, and
    most preferably not stable at >20°; (8) a base other than U at
    position 5; and (9) a base other than A at position 11. Sequence features
     in siRNA that promote functionality were identified using an siRNA panel
     consisting of 270 siRNAs targeting three genes: human cyclophilin, firefly
     luciferase, and human diazepam-binding inhibitor. Bcl-2 siRNAs
     having the top ten "SMARTscores®" according to the selection
     algorithms, were selected and tested in a functional assay to determine
     silencing efficiency. Genome-wide application of the algorithm was
     accomplished by processing the entire online NCBI RefSeg database through
     Formula VIII; the top 80-100 scores for siRNAs are obtained and BLAST'ed
     to entire that the selected sequences are specific in targeting the gene
                [This abstract record is one of 281 records for this document
    necessitated by the large number of index entries required to fully index the
     document and publication system constraints.].
ST
     siRNA selection algorithm gene silencing
IT
    Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (Bcl-2; algorithms for rational design and selection of functional and
       hyperfunctional siRNA for gene silencing)
ΙT
    Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (DBI (diazepam binding inhibitor); algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
    Algorithm
    Drug design
     Optimization
        (algorithms for rational design and selection of functional and
        hyperfunctional siRNA for gene silencing)
ΙT
     Cyclophilins
```

- RL: BSU (Biological study, unclassified); BIOL (Biological study) (algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT Gene targeting
 (gene knock-out; algorithms for rational design and selection of
 functional and hyperfunctional siRNA for gene silencing)
- IT Post-transcriptional processing
 (gene silencing; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- (genome-wide application; algorithms for rational design and selection
 of functional and hyperfunctional siRNA for gene silencing)
 IT Post-transcriptional processing
- (interference; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

IT

Human

- IT RNA sequences

 (of siRNAs rationally designed for human genes; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT Double stranded RNA
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (small interfering; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 61970-00-1, Firefly luciferase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694204-51-8P 694204-52-9P 694215-84-4P 694221-17-5P 694221-18-6P 694221-19-7P 694221-20-0P 694221-21-1P 694221-22-2P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of -specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694205-25-9P 694205-26-0P 694205-27-1P 694205-28-2P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)

- (nucleotide sequence of ABL1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694219-20-0P 694219-21-1P 694219-22-2P 694219-23-3P 694219-24-4P 694219-25-5P 694219-26-6P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of AIF1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694204-09-6P 694204-10-9P 694204-11-0P 694204-12-1P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of AKT3-specific siRNA; algorithms for rational
 design and selection of functional and hyperfunctional siRNA for gene
 silencing)

- IT 694217-93-1P 694217-94-2P 694217-95-3P 694217-96-4P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

TT

ΙT

IT

IT

IT

IT

ΙT

IT

TT

silencing)

```
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of ARHA-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694222-67-8P
               694222-68-9P
                              694222-69-0P
                                             694222-70-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of ARX-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694203-60-6P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of ATE1-1-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694203-61-7P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of ATE1-2-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694203-62-8P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of ATE1-3-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694203-63-9P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of ATE1-4-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694208-56-5P
               694208-57-6P
                              694208-58-7P
                                             694208-59-8P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of ATM-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694208-60-1P
               694208-61-2P
                              694208-62-3P
                                             694208-63-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of ATR-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694205-41-9P
               694205-42-0P
                              694205-43-1P
                                             694205-44-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of AXL-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694222-48-5P
               694222-49-6P
                              694222-50-9P
                                             694222-51-0P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of BACE1-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
```

IT 694216-87-0P 694216-88-1P 694216-89-2P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

```
PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of BAD-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694219-27-7P
                    694219-28-8P
                                   694219-29-9P
                                                  694219-30-2P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of BBC3-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694219-31-3P
                    694219-32-4P
                                   694219-33-5P
                                                  694219-34-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of BCL2L1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
     694219-35-7P
                    694219-36-8P
                                   694219-37-9P
                                                  694219-38-0P
                                                                 694219-39-1P
     694219-40-4P
                    694219-41-5P
                                   694219-42-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of BCL2L11-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-50-4P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of BCL2_1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
     694203-51-5P
TT
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of BCL2_2-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
ΙT
     694203-52-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of BCL2_3-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-53-7P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of BCL2_4-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
     694203-54-8P
IT
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of BCL2_5-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
    694203-55-9P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of BCL2_6-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
ΙT
     694219-43-7P
                    694219-44-8P
                                   694219-45-9P
                                                  694219-46-0P
```

- RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of BID-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694217-13-5P 694217-14-6P 694217-15-7P 694217-16-8P 694217-17-9P 694217-18-0P

 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of BRCA1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694202-32-9P 694202-33-0P 694202-34-1P 694202-35-2P 694202-36-3P 694202-37-4P 694202-38-5P 694202-39-6P 694202-40-9P 694202-41-0P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of Bcl2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694219-67-5P 694219-68-6P 694219-69-7P 694219-70-0P 694219-71-1P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of CASP10-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694219-72-2P 694219-73-3P 694219-74-4P 694219-75-5P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of CASP2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene

```
silencing)
```

silencing)

- IT 694216-17-6P 694216-18-7P 694216-19-8P 694216-20-1P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 - (nucleotide sequence of CASP3-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694216-21-2P 694216-22-3P 694216-23-4P 694216-24-5P 694216-25-6P 694216-26-7P
 - RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of CASP6-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene
 - design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694216-31-4P 694216-32-5P 694216-33-6P 694216-34-7P 694216-35-8P 694216-36-9P 694216-37-0P 694216-38-1P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of CASP8-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene

- IT 694208-76-9P 694208-77-0P 694208-78-1P 694208-79-2P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)

- (nucleotide sequence of CCNB1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694209-16-0P 694209-17-1P 694209-18-2P 694209-19-3P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)

```
(nucleotide sequence of CCNG1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
```

- IT 694209-32-0P 694209-33-1P 694209-34-2P 694209-35-3P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of CCNT1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694209-49-9P 694209-50-2P 694209-51-3P 694209-52-4P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)

- (nucleotide sequence of CDC20-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694217-97-5P 694217-98-6P 694217-99-7P 694218-00-3P 694218-01-4P 694218-02-5P 694218-03-6P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of CDC42-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694209-77-3P 694209-78-4P 694209-79-5P 694209-80-8P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of CDC45L-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694209-85-3P 694209-86-4P 694209-87-5P 694209-88-6P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of CDC7-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694217-19-1P 694217-20-4P 694217-21-5P 694217-22-6P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of CDKN1A-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694210-56-5P 694210-57-6P 694210-58-7P 694210-59-8P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of CENPE-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694202-46-5P 694202-47-6P 694202-48-7P 694202-49-8P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of CLTA-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694219-88-0P 694219-89-1P 694219-90-4P 694219-91-5P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of CSNK2A1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694203-31-1P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of DBI2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694203-32-2P
 - RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of DBI3-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694203-33-3P
 - RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of DBI4-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694210-84-9P 694210-85-0P 694210-86-1P 694210-87-2P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of E2F1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694210-96-3P 694210-97-4P 694210-98-5P 694210-99-6P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of E2F4-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694203-64-0P 694203-65-1P 694203-66-2P 694203-67-3P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

IT

for gene silencing)

694206-09-2P

694206-10-5P

```
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of EGFR-1-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694204-21-2P
               694204-22-3P
                              694204-23-4P
                                             694204-24-5P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of EIF4EBP1-specific siRNA; algorithms for
   rational design and selection of functional and hyperfunctional siRNA
   for gene silencing)
694218-89-8P
               694218-90-1P
                              694218-91-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of ELK1-specific siRNA; algorithms for rational
   design and selection of functional and hyperfunctional siRNA for gene
   silencing)
694205-81-7P
                                             694205-84-0P
               694205-82-8P
                              694205-83-9P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of EPHA1-specific siRNA; algorithms for
   rational design and selection of functional and hyperfunctional siRNA
   for gene silencing)
694205-85-1P
               694205-86-2P
                              694205-87-3P
                                             694205-88-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of EPHA2-specific siRNA; algorithms for
   rational design and selection of functional and hyperfunctional siRNA
   for gene silencing)
694205-89-5P
               694205-90-8P
                              694205-91-9P
                                             694205-92-0P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of EPHA3-specific siRNA; algorithms for
   rational design and selection of functional and hyperfunctional siRNA
   for gene silencing)
                              694205-95-3P
694205-93-1P
               694205-94-2P
                                             694205-96-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of EPHA4-specific siRNA; algorithms for
   rational design and selection of functional and hyperfunctional siRNA
   for gene silencing)
694205-97-5P
               694205-98-6P
                              694205-99-7P
                                             694206-00-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of EPHA7-specific siRNA; algorithms for
   rational design and selection of functional and hyperfunctional siRNA
   for gene silencing)
694206-01-4P
               694206-02-5P
                              694206-03-6P
                                             694206-04-7P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of EPHA8-specific siRNA; algorithms for
   rational design and selection of functional and hyperfunctional siRNA
   for gene silencing)
694206-05-8P
              694206-06-9P
                             694206-07-0P
                                           694206-08-1P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
   (nucleotide sequence of EPHB1-specific siRNA; algorithms for
```

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

694206-12-7P

694206-11-6P

rational design and selection of functional and hyperfunctional siRNA

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of EPHB2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694206-25-2P 694206-26-3P 694206-27-4P 694206-28-5P 694217-05-5P 694217-06-6P 694217-07-7P 694217-08-8P

 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of ERBB2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694213-02-0P 694213-03-1P 694213-04-2P 694213-05-3P

- RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of ESR2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694206-49-0P 694206-50-3P 694206-51-4P 694206-52-5P

- RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of FGFR2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694206-61-6P 694206-62-7P 694206-63-8P 694206-64-9P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of FGR-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694217-39-5P 694217-40-8P 694217-41-9P 694217-42-0P 694217-43-1P 694217-44-2P

 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of FKBP1A-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694204-33-6P 694204-34-7P 694204-35-8P 694204-36-9P 694217-35-1P 694217-36-2P 694217-37-3P 694217-38-4P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of FRAP1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694203-97-9P 694203-98-0P 694203-99-1P 694204-00-7P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of GLUT12-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene

- IT 694218-60-5P 694218-61-6P 694218-62-7P 694218-63-8P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of GRB2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694220-16-1P 694220-17-2P 694220-18-3P 694220-19-4P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of HDAC3-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene

```
silencing)
IT
     694220-20-7P
                    694220-21-8P
                                   694220-22-9P
                                                  694220-23-0P
                                                                  694220-24-1P
     694220-25-2P
                    694220-26-3P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of HDAC5-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
TT
     694221-83-5P
                    694221-84-6P
                                   694221-85-7P
                                                  694221-86-8P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of HDC-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694220-27-4P
                    694220-28-5P
                                   694220-29-6P
                                                  694220-30-9P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of HEC-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-76-4P
                    694203-77-5P
                                   694203-78-6P
                                                  694203-79-7P
                                                                 694203-80-0P
     694203-81-1P
                    694203-82-2P · 694203-83-3P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of HIF-1\alpha-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
     694211-12-6P
IT
                    694211-13-7P
                                   694211-14-8P
                                                  694211-15-9P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of HIPK2-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694220-31-0P
                    694220-32-1P
                                   694220-33-2P
                                                  694220-34-3P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of HIST1H2AA-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
                    694222-08-7P
IT
     694222-07-6P
                                   694222-09-8P
                                                  694222-10-1P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of HMB-CoA reductase-specific siRNA; algorithms
        for rational design and selection of functional and hyperfunctional
        siRNA for gene silencing)
IT
     694213-18-8P
                    694213-19-9P
                                   694213-20-2P
                                                  694213-21-3P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of HNF4A-specific siRNA; algorithms for rational
       design and selection of functional and hyperfunctional siRNA for gene
       silencing)
ΙT
    694213-22-4P
                    694213-23-5P
                                   694213-24-6P
                                                  694213-25-7P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of HNG4G-specific siRNA; algorithms for rational
       design and selection of functional and hyperfunctional siRNA for gene
```

694218-85-4P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

PRP (Properties); BIOL (Biological study); PREP (Preparation)

silencing)

694218-84-3P

694218-83-2P

IT

- (nucleotide sequence of HRAS-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694204-45-0P 694204-46-1P 694204-47-2P 694204-48-3P 694204-50-7P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of IGF1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694204-53-0P 694204-54-1P 694204-55-2P 694204-56-3P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)

- (nucleotide sequence of INPP5D-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694211-20-6P 694211-21-7P 694211-22-8P 694211-23-9P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)

```
(nucleotide sequence of JUN-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
```

- IT 694215-02-6P 694215-03-7P 694215-04-8P 694215-05-9P 694215-06-0P 694215-07-1P 694215-08-2P 694215-09-3P

 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of KCNH2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694207-16-4P 694207-17-5P 694207-18-6P 694207-19-7P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

1

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of LCK-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694211-28-4P 694211-29-5P 694211-30-8P 694211-31-9P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of LOC51053-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694219-00-6P 694219-01-7P 694219-02-8P 694219-03-9P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of MAP2K4-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694219-04-0P 694219-05-1P 694219-06-2P 694219-07-3P 694219-08-4P 694219-09-5P 694219-10-8P 694219-11-9P
 - RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 - PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of MAP2K7-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694211-52-4P 694211-53-5P 694211-54-6P 694211-55-7P

- RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of MCM5-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694207-44-8P 694207-45-9P 694207-46-0P 694207-47-1P

- RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of MUSK-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694213-38-2P 694213-39-3P 694213-40-6P 694213-41-7P

- RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of NR1D1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694213-78-0P 694213-79-1P 694213-80-4P 694213-81-5P 694213-83-7P

```
694213-85-9P
     694213-84-8P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of NR2F1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694213-82-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of NR2F2-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694213-86-0P
                    694213-87-1P
                                   694213-88-2P
                                                  694213-89-3P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of NR2F6-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
     694213-90-6P
                    694213-91-7P
                                   694213-92-8P
IT
                                                  694213-93-9P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of NR3C1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
TT
     694213-94-0P
                    694213-95-1P
                                   694213-96-2P
                                                  694213-97-3P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of NR3C2-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
                    694213-99-5P
                                   694214-00-1P
IT
     694213-98-4P
                                                  694214-01-2P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of NR4A1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694214-02-3P
                    694214-03-4P
                                   694214-04-5P
                                                  694214-05-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of NR4A2-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694214-06-7P
                    694214-07-8P
                                   694214-08-9P
                                                  694214-09-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of NR4A3-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694214-10-3P
                                   694214-12-5P
                    694214-11-4P
                                                  694214-13-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of NR5A1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694214-14-7P
                    694214-15-8P
                                   694214-16-9P
                                                  694214-17-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
```

(nucleotide sequence of NR5A2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene

PRP (Properties); BIOL (Biological study); PREP (Preparation)

- IT 694218-24-1P 694218-25-2P 694218-26-3P 694218-27-4P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of PAK6-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694203-88-8P 694203-89-9P 694203-90-2P 694203-91-3P 694203-92-4P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of PDGF B-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694207-60-8P 694207-61-9P 694207-62-0P 694207-63-1P 694207-64-2P 694207-65-3P 694207-66-4P 694207-67-5P

 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of PDGFRA-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694212-14-1P 694212-15-2P 694212-16-3P 694212-17-4P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of PIN1L-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene

```
haddad - 10 / 823259
        silencing)
IT
     694218-64-9P
                    694218-65-0P
                                   694218-66-1P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of PLCG1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
     694202-94-3P
                    694202-95-4P
                                   694202-96-5P
                                                  694202-97-6P
IT
                                                                 694212-07-2P
                    694212-09-4P
     694212-08-3P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of PLK-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694214-30-7P
                    694214-31-8P
                                   694214-32-9P
                                                  694214-33-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of PPARA-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
ΙT
     694214-34-1P
                    694214-35-2P
                                   694214-36-3P
                                                  694214-37-4P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of PPARD-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694214-38-5P
                    694214-39-6P
                                   694214-40-9P
                                                  694214-41-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of PPARG-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694216-63-2P
                    694216-64-3P
                                   694216-65-4P
                                                  694216-66-5P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of PPP2CA-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694204-89-2P
                    694204-90-5P
                                   694204-91-6P
                                                  694204-92-7P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of PPP2R2B-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
     694218-96-7P
IT
                    694218-97-8P
                                   694218-98-9P
                                                  694218-99-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of PRKCA-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694220-82-1P
                    694220-83-2P
                                   694220-84-3P
                                                  694220-85-4P
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of PRKDC-specific siRNA; algorithms for rational
       design and selection of functional and hyperfunctional siRNA for gene
```

694222-54-3P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

PRP (Properties); BIOL (Biological study); PREP (Preparation)

694222-55-4P

694222-56-5P

silencing)

694222-53-2P

694222-58-7P

694222-52-1P

694222-57-6P

IT

```
(nucleotide sequence of PSEN1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
```

- IT 694204-93-8P 694204-94-9P 694204-95-0P 694204-96-1P 694216-51-8P 694216-52-9P 694216-53-0P 694216-54-1P

 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of PTEN-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694207-80-2P 694207-81-3P 694207-82-4P 694207-83-5P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of PTK7-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694217-01-1P 694217-02-2P 694217-03-3P 694217-04-4P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

```
PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of PVR-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-56-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of QB1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-57-1P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of QB2-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
     694203-58-2P
IT
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of QB3-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
TT
     694203-59-3P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of QB4-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694202-74-9P
                    694202-75-0P
                                   694202-76-1P
                                                  694202-77-2P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of RAB5A-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
                    694202-79-4P
IT
     694202-78-3P
                                   694202-80-7P
                                                  694202-81-8P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of RAB5B-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694202-82-9P
                    694202-83-0P
                                   694202-84-1P
                                                  694202-85-2P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of RAB5C-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694212-18-5P
                    694212-19-6P
                                   694212-20-9P
                                                  694212-21-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of RAD1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694212-22-1P
                    694212-23-2P
                                   694212-24-3P
                                                  694212-25-4P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of RAD17-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
```

694212-28-7P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

694212-29-8P

silencing)

694212-27-6P

694212-26-5P

IT

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of RAD9A-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694212-46-9P 694212-47-0P 694212-48-1P 694212-49-2P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of RBP1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694208-04-3P 694208-05-4P 694208-06-5P 694208-07-6P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of ROS1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694212-50-5P 694212-51-6P 694212-52-7P 694212-53-8P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation) '
 (nucleotide sequence of RPA3-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694212-54-9P 694212-55-0P 694212-56-1P 694212-57-2P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

- PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of SKP1A-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694215-30-0P 694215-31-1P 694215-32-2P 694215-33-3P 694215-34-4P 694215-35-5P 694215-36-6P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of SLC21Z3-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

694215-43-5P

694215-44-6P

694215-45-7P

694215-42-4P

IT

694215-41-3P

- 694215-46-8P 694215-47-9P 694215-48-0P 694215-49-1P 694215-50-4P 694215-51-5P 694215-52-6P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of SLC29A1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

```
silencing)
```

- IT 694215-22-0P 694215-23-1P 694215-24-2P 694215-25-3P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of SLC6A2-specific siRNA; algorithms for rational
 - (nucleotide sequence of SLC6A2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694220-90-1P 694220-91-2P 694220-92-3P 694220-93-4P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of SLC9A1-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene
- silencing)
 IT 694216-90-5P 694216-91-6P 694216-92-7P 694216-93-8P 694216-94-9P 694216-95-0P 694216-96-1P
 - RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of SMAC-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694221-99-3P 694222-00-9P 694222-01-0P 694222-02-1P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of STAT6-specific siRNA; algorithms for rational

```
design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694212-66-3P
                    694212-67-4P 694212-68-5P
                                                  694212-69-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of STK12-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694208-67-8P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of STK6-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694208-16-7P
                    694208-17-8P
                                   694208-18-9P
                                                  694208-19-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of SYK-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-38-8P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of SeAP1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-39-9P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of SeAP2-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-40-2P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of SeAP3-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-41-3P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of SeAP4-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694221-71-1P
                    694221-72-2P
                                   694221-73-3P
                                                  694221-74-4P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of TAP1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694208-20-3P
                    694208-21-4P
                                   694208-22-5P
                                                  694208-23-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of TEC-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
                    694220-95-6P
ΙT
     694220-94-5P
                                   694220-96-7P
                                                  694220-97-8P
```

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

(nucleotide sequence of TEGT-specific siRNA; algorithms for rational

PRP (Properties); BIOL (Biological study); PREP (Preparation)

- design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694208-24-7P 694208-25-8P 694208-26-9P 694208-27-0P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (nucleotide sequence of TEK-specific siRNA; algorithms for rational

(nucleotide sequence of TEK-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694217-84-0P 694217-85-1P 694217-86-2P 694217-87-3P 694217-88-4P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of TNFRSF5-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694221-02-8P 694221-03-9P 694221-04-0P 694221-05-1P 694221-06-2P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of TNFRSF6-specific siRNA; algorithms for rational

- design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694221-11-9P 694221-12-0P 694221-13-1P 694221-14-2P 694221-16-4P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of TOP2A-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694217-66-8P 694217-67-9P 694217-68-0P 694217-69-1P 694217-70-4P
 694217-71-5P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 - PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of TRADD-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694217-57-7P 694217-58-8P 694217-59-9P 694217-60-2P 694217-61-3P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation) (nucleotide sequence of TRAF2-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)
- IT 694217-62-4P 694217-63-5P 694217-64-6P 694217-65-7P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)

- (nucleotide sequence of TRAF6-specific siRNA; algorithms for rational design and selection of functional and hyperfunctional siRNA for gene silencing)

- IT 694215-73-1P 694215-74-2P 694215-75-3P 694215-76-4P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)

```
(nucleotide sequence of XPNPEP1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694205-21-5P
                    694205-22-6P
                                   694205-23-7P
                                                  694205-24-8P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of XPO1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694208-48-5P
                    694208-49-6P
                                   694208-50-9P
                                                  694208-51-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of YES1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694212-90-3P
                    694212-91-4P
                                   694212-92-5P
                                                  694212-93-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of YWHAZ-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694221-58-4P
                    694221-59-5P
                                   694221-60-8P
                                                  694221-61-9P
                                                                  694221-62-0P
     694221-63-1P
                    694221-64-2P
                                   694221-65-3P
                                                  694221-66-4P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of activin A receptor IB-specific siRNA;
        algorithms for rational design and selection of functional and
        hyperfunctional siRNA for gene silencing)
IT
     694222-75-8P
                    694222-76-9P
                                   694222-77-0P
                                                  694222-78-1P
                                                                 694222-79-2P
     694222-80-5P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of angiotensin II type 1 receptor
        -specific siRNA; algorithms for rational design and selection of
        functional and hyperfunctional siRNA for gene silencing)
IT
     694203-02-6P
                    694203-03-7P
                                   694203-04-8P
                                                  694203-05-9P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of c-Myc-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
     694203-18-4P
                    694203-19-5P
IT
                                   694203-20-8P
                                                  694203-21-9P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of cyclophilin A-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
IT
     694203-26-4P
                    694203-27-5P
                                   694203-28-6P
                                                  694203-29-7P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of cyclophilin B-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
IT
     694199-63-8P
                    694199-64-9P
                                   694199-65-0P
                                                  694199-66-1P
                                                                 694199-67-2P
     694199-68-3P
                    694199-69-4P
                                   694199-70-7P
                                                  694199-71-8P
                                                                 694199-72-9P
     694199-73-0P
                    694199-74-1P
                                   694199-75-2P
                                                  694199-76-3P
                                                                 694199-77-4P
     694199-78-5P
                    694199-79-6P
                                   694199-80-9P
                                                  694199-81-0P
                                                                 694199-82-1P
     694199-83-2P
                    694199-84-3P
                                   694199-85-4P
                                                  694199-86-5P
                                                                 694199-87-6P
     694199-88-7P
                    694199-89-8P
                                   694199-90-1P
                                                  694199-91-2P
                                                                 694199-92-3P
     694199-93-4P
                    694199-94-5P
                                   694199-95-6P
                                                  694199-96-7P
                                                                 694199-97-8P
```

```
694199-98-9P
                    694199-99-0P
                                   694200-00-5P
                                                  694200-01-6P
                                                                 694200-02-7P
     694200-03-8P
                    694200-04-9P
                                   694200-05-0P
                                                  694200-06-1P
                                                                 694200-07-2P
     694200-08-3P
                    694200-09-4P
                                   694200-10-7P
                                                  694200-11-8P
                                                                 694200-12-9P
     694200-13-0P
                    694200-14-1P
                                   694200-15-2P
                                                  694200-16-3P
                                                                 694200-17-4P
                                   694200-20-9P
                    694200-19-6P
     694200-18-5P
                                                  694200-21-0P
                                                                 694200-22-1P
                    694200-24-3P
     694200-23-2P
                                   694200-25-4P
                                                  694200-26-5P
                                                                 694200-27-6P
     694200-28-7P
                    694200-29-8P
                                   694200-30-1P
                                                  694200-31-2P
                                                                 694200-32-3P
     694200-33-4P
                    694200-34-5P
                                   694200-35-6P
                                                  694200-36-7P
                                                                 694200-37-8P
     694200-38-9P
                    694200-39-0P
                                   694200-40-3P
                                                  694200-41-4P
                                                                 694200-42-5P
     694200-43-6P
                    694200-44-7P
                                   694200-45-8P
                                                  694200-46-9P
                                                                 694200-47-0P
                                                  694200-51-6P
     694200-48-1P
                    694200-49-2P
                                   694200-50-5P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of cyclophilin-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
IT
     694200-52-7P
                    694200-53-8P
                                   694200-54-9P
                                                  694200-55-0P
                                                                 694200-56-1P
     694200-57-2P
                    694200-58-3P
                                   694200-59-4P
                                                  694200-60-7P
                                                                 694200-61-8P
                    694200-63-0P
     694200-62-9P
                                   694200-64-1P
                                                  694200-65-2P
                                                                 694200-66-3P
                    694200-68-5P
                                                  694200-70-9P
     694200-67-4P
                                   694200-69-6P
                                                                 694200-71-0P
                                                  694200-75-4P
                    694200-73-2P
                                   694200-74-3P
     694200-72-1P
                                                                 694200-76-5P
                    694200-78-7P
                                   694200-79-8P
                                                                 694200-81-2P
     694200-77-6P
                                                  694200-80-1P
                                                                 694200-86-7P
     694200-82-3P
                    694200-83-4P
                                   694200-84-5P
                                                  694200-85-6P
     694200-87-8P
                    694200-88-9P
                                   694200-89-0P
                                                  694200-90-3P
                                                                 694200-91-4P
     694200-92-5P
                    694200-93-6P
                                   694200-94-7P
                                                  694200-95-8P
                                                                 694200-96-9P
                    694200-98-1P
     694200-97-0P
                                   694200-99-2P
                                                  694201-00-8P
                                                                 694201-01-9P
                    694201-03-1P
                                   694201-04-2P
                                                                 694201-06-4P
     694201-02-0P
                                                  694201-05-3P
     694201-07-5P
                    694201-08-6P
                                   694201-09-7P
                                                  694201-10-0P
                                                                 694201-11-1P
     694201-12-2P
                    694201-13-3P
                                   694201-14-4P
                                                  694201-15-5P
                                                                 694201-16-6P
     694201-17-7P
                    694201-18-8P
                                   694201-19-9P
                                                  694201-20-2P
                                                                 694201-21-3P
                                                                 694201-26-8P
                    694201-23-5P
     694201-22-4P
                                   694201-24-6P
                                                  694201-25-7P
                                                                 694201-31-5P
     694201-27-9P
                    694201-28-0P
                                   694201-29-1P
                                                  694201-30-4P
                    694201-33-7P
                                   694201-34-8P
                                                  694201-35-9P
     694201-32-6P
                                                                 694201-36-0P
     694201-37-1P
                    694201-38-2P
                                   694201-39-3P
                                                  694201-40-6P
                                                                 694201-41-7P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of diazepam binding inhibitor-specific
        siRNA; algorithms for rational design and selection of functional and
        hyperfunctional siRNA for gene silencing)
IT
     694203-42-4P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of fLUC1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-43-5P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of fLUC2-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-44-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of fLUC3-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-45-7P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
```

```
(nucleotide sequence of fLUC4-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
                                   694222-39-4P
IT
     694222-37-2P
                    694222-38-3P
                                                  694222-40-7P
                                                                 694222-41-8P
     694222-42-9P
                    694222-43-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of factor VIII-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
IT
     694201-42-8P
                    694201-43-9P
                                   694201-44-0P
                                                  694201-45-1P
                                                                 694201-46-2P
     694201-47-3P
                    694201-48-4P
                                   694201-49-5P
                                                  694201-50-8P
                                                                 694201-51-9P
     694201-52-0P
                    694201-53-1P
                                   694201-54-2P
                                                  694201-55-3P
                                                                 694201-56-4P
     694201-57-5P
                    694201-58-6P
                                   694201-59-7P
                                                  694201-60-0P
                                                                 694201-61-1P
     694201-62-2P
                    694201-63-3P
                                   694201-64-4P
                                                  694201-65-5P
                                                                 694201-66-6P
     694201-67-7P
                    694201-68-8P
                                   694201-69-9P
                                                  694201-70-2P
                                                                 694201-71-3P
     694201-72-4P
                    694201-73-5P
                                   694201-74-6P
                                                  694201-75-7P
                                                                 694201-76-8P
     694201-77-9P
                   694201-78-0P
                                   694201-79-1P
                                                  694201-80-4P
                                                                 694201-81-5P
     694201-82-6P
                   694201-83-7P
                                   694201-84-8P
                                                  694201-85-9P
                                                                 694201-86-0P
     694201-87-1P
                   694201-88-2P
                                   694201-89-3P
                                                  694201-90-6P
                                                                 694201-91-7P
     694201-92-8P
                   694201-93-9P
                                   694201-94-0P
                                                  694201-95-1P
                                                                 694201-96-2P
     694201-97-3P
                    694201-98-4P
                                   694201-99-5P
                                                  694202-00-1P
                                                                 694202-01-2P
     694202-02-3P
                    694202-03-4P
                                   694202-04-5P
                                                                 694202-06-7P
                                                  694202-05-6P
     694202-07-8P
                    694202-08-9P
                                   694202-09-0P
                                                  694202-10-3P
                                                                 694202-11-4P
     694202-12-5P
                    694202-13-6P
                                   694202-14-7P
                                                  694202-15-8P
                                                                 694202-16-9P
     694202-17-0P
                    694202-18-1P
                                   694202-19-2P
                                                  694202-20-5P
                                                                 694202-21-6P
     694202-22-7P
                    694202-23-8P
                                   694202-24-9P.
                                                  694202-25-0P
                                                                 694202-26-1P
     694202-27-2P
                    694202-28-3P
                                   694202-29-4P
                                                  694202-30-7P
                                                                 694202-31-8P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of firefly luciferase-specific siRNA; algorithms
        for rational design and selection of functional and hyperfunctional
        siRNA for gene silencing)
IT
     694203-72-0P
                    694203-73-1P
                                   694203-74-2P
                                                  694203-75-3P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of glutamine: fructose 6-phosphate
        aminotransferase-specific siRNA; algorithms for rational design and
        selection of functional and hyperfunctional siRNA for gene silencing)
IT
     694221-34-6P
                    694221-35-7P
                                  694221-36-8P
                                                  694221-37-9P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of interferon \gamma receptor
        1-specific siRNA; algorithms for rational design and selection of
        functional and hyperfunctional siRNA for gene silencing)
IT
     694221-27-7P
                    694221-28-8P
                                   694221-29-9P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of interleukin 4 receptor-specific
        siRNA; algorithms for rational design and selection of functional and
        hyperfunctional siRNA for gene silencing)
IT
     694203-22-0P
                    694203-23-1P
                                   694203-24-2P
                                                  694203-25-3P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of lamin A/C-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
IT
     694203-46-8P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
```

```
(nucleotide sequence of mCyclo_1-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
TΤ
     694203-47-9P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of mCyclo 2-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
     694203-48-0P
IT
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of mCyclo_3-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
IT
     694203-49-1P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of mCyclo_4-specific siRNA; algorithms for
        rational design and selection of functional and hyperfunctional siRNA
        for gene silencing)
     694221-38-0P
                    694221-39-1P
                                   694221-40-4P
                                                  694221-41-5P
TT
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of matrix metalloproteinase MMP-9-specific siRNA;
        algorithms for rational design and selection of functional and
        hyperfunctional siRNA for gene silencing)
IT
                   694199-33-2
                                 694199-34-3
                                               694199-35-4
                                                             694199-36-5
     694199-32-1
     694199-37-6
                   694199-38-7
                               694199-39-8
                                               694199-40-1
                                                             694199-41-2
                  694199-43-4 694199-44-5
     694199-42-3
                                               694199-45-6
                                                             694199-46-7
                  694199-48-9 694199-49-0
                                               694199-50-3
                                                             694199-51-4
     694199-47-8
                  694199-53-6 694199-54-7
                                               694199-55-8
                                                             694199-56-9
     694199-52-5
     694199-57-0
                  694199-58-1 694199-59-2
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (nucleotide sequence of optimized siRNA; algorithms for rational design
        and selection of functional and hyperfunctional siRNA for gene
        silencing)
TT
     694203-34-4P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of rLUC1-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
     694203-35-5P
TΥ
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of rLUC2-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694203-36-6P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of rLUC3-specific siRNA; algorithms for rational
        design and selection of functional and hyperfunctional siRNA for gene
        silencing)
TT
     694203-37-7P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of rLUC4-specific siRNA; algorithms for rational
```

```
design and selection of functional and hyperfunctional siRNA for gene
        silencing)
IT
     694199-60-5
                                 694199-62-7
                   694199-61-6
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (nucleotide sequence of siRNA target; algorithms for rational design
        and selection of functional and hyperfunctional siRNA for gene
        silencing)
     694214-22-7P
                    694214-23-8P
                                   694214-24-9P
IT
                                                  694214-25-0P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of siRNA; algorithms for rational design and
        selection of functional and hyperfunctional siRNA for gene silencing)
ΙT
     694221-54-0P
                    694221-55-1P
                                   694221-56-2P
                                                 694221-57-3P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of thymosin β4Y-specific siRNA; algorithms
        for rational design and selection of functional and hyperfunctional
        siRNA for gene silencing)
IT
     694221-30-2P
                   694221-31-3P
                                   694221-32-4P
                                                 694221-33-5P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); BIOL (Biological study); PREP (Preparation)
        (nucleotide sequence of \beta-arrestin 2-specific siRNA; algorithms
        for rational design and selection of functional and hyperfunctional
        siRNA for gene silencing)
IT
     694224-43-6
                   694224-44-7
                                 694224-47-0
                                               694224-48-1
                                                             694224-49-2
     694224-50-5
                   694224-51-6
                                 694224-52-7
                                               694224-53-8
                                                             694224-54-9
     RL: PRP (Properties)
        (unclaimed sequence; algorithms for rational design and selection of
        functional and hyperfunctional siRNA for gene silencing)
    ANSWER 7 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2004:287786 HCAPLUS
DN
     140:315100
ED
     Entered STN: 08 Apr 2004
     Agents that modulate Eph receptor activity,
TI
     therapeutic use, and screening methods
IN
     Pasquale, Elena B.; Koolpe, Mitchell; Murai, Keith K.
PA
     The Burnham Institute, USA
     PCT Int. Appl., 97 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
IC
     ICM A61K038-00
     ICS G01N033-53; C07K014-00
     1-12 (Pharmacology)
     Section cross-reference(s): 63
FAN.CNT 1
     PATENT NO.
                         KIND
                              DATE
                                           APPLICATION NO.
                                                                   DATE
                         ----
                                -----
                                            ------
                                                                   _____
PΙ
     WO 2004028551
                         A1
                                20040408
                                           WO 2003-US27328
                                                                   20030829 <--
     WO 2004028551
                         C2
                                20040701
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
```

```
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    US 2004180823
                               20040916 US 2003-652407
                         A1
                                                                 20030829 <--
PRAI US 2002-413242P
                         P
                               20020924 <--
CLASS
               CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
                ----
 -----
                       _______
 WO 2004028551
                ICM
                       A61K038-00
                ICS
                       G01N033-53; C07K014-00
WO 2004028551
                ECLA
                       A61K047/48R2; A61K049/00F; C07K014/52; G01N033/68D <--
US 2004180823
                NCL
                       514/012.000; 530/350.000
                ECLA
                       A61K049/00F; G01N033/68D
                                                                           <--
    Agents are described that bind to Eph receptors.
AB
    Methods of using these agents to modulate the activity of Eph
    receptors, stimulate apoptosis, and deliver therapeutic agents are
     also described. Methods of screening for agents capable of selectively
    binding to Eph receptors are also described.
ST
     Eph receptor ligand screening therapeutic delivery
     apoptosis
ΙT
     Tyrosine kinase receptors
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (Eph receptor; agents modulating Eph
       receptor activity, therapeutic use, and screening methods)
TT
    Antitumor agents
    Apoptosis
    Drug delivery systems
    Drug screening
    Human
    Mental retardation
    NMR spectroscopy
    Neoplasm
    Nervous system agents
    Peptide library
    Peptidomimetics
     Phage display library
     Signal transduction, biological
        (agents modulating Eph receptor activity,
        therapeutic use, and screening methods)
IT
     Isotopomers
    Ligands
    Peptides, biological studies
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (agents modulating Eph receptor activity,
       therapeutic use, and screening methods)
IT
    NMR spectroscopy
        (carbon-13; agents modulating Eph receptor
       activity, therapeutic use, and screening methods)
IT
     Imaging agents
        (conjugates with Eph receptor ligands; agents
       modulating Eph receptor activity, therapeutic use,
       and screening methods)
IT
    Nerve, disease
    Nervous system, disease
        (degeneration; agents modulating Eph receptor
       activity, therapeutic use, and screening methods)
IT
    Proteins
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin A; agents modulating Eph receptor
       activity, therapeutic use, and screening methods)
```

```
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin B4; agents modulating Eph receptor
        activity, therapeutic use, and screening methods)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor 1; agents modulating
        Eph receptor activity, therapeutic use, and screening
        methods)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor
        2; agents modulating Eph receptor activity,
        therapeutic use, and screening methods)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor 3; agents modulating
        Eph receptor activity, therapeutic use, and screening
        methods)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor 4; agents modulating
        Eph receptor activity, therapeutic use, and screening
        methods)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor 5; agents modulating
        Eph receptor activity, therapeutic use, and screening
        methods)
     Tyrosine kinase receptors
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor, EphA6; agents
        modulating Eph receptor activity, therapeutic use,
        and screening methods)
ΙT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor, EphA7; agents
        modulating Eph receptor activity, therapeutic use,
        and screening methods)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor, EphA8; agents
        modulating Eph receptor activity, therapeutic use,
        and screening methods)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-B receptor 1; agents modulating
        Eph receptor activity, therapeutic use, and screening
        methods)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-B receptor 6; agents modulating
        Eph receptor activity, therapeutic use, and screening
        methods)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-B receptor, EphB2; agents
        modulating Eph receptor activity, therapeutic use,
        and screening methods)
```

IT

Tyrosine kinase receptors

```
RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-B receptor, EphB3; agents
        modulating Eph receptor activity, therapeutic use,
        and screening methods)
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin; agents modulating Eph receptor
        activity, therapeutic use, and screening methods)
IT
    NMR spectroscopy
        (fluorine-19; agents modulating Eph receptor
        activity, therapeutic use, and screening methods)
IT
     Regeneration, animal
        (nerve; agents modulating Eph receptor activity,
        therapeutic use, and screening methods)
IT
    NMR (nuclear magnetic resonance)
        (nitrogen-15; agents modulating Eph receptor
        activity, therapeutic use, and screening methods)
IT
     Phosphorylation, biological
        (protein; agents modulating Eph receptor
        activity, therapeutic use, and screening methods)
IT
        (regeneration; agents modulating Eph receptor
        activity, therapeutic use, and screening methods)
IT
     Therapy
        (therapeutic agent-Eph receptor ligand conjugates;
        agents modulating Eph receptor activity,
        therapeutic use, and screening methods)
IT
     Injury
        (trauma, traumatic injury; agents modulating Eph
        receptor activity, therapeutic use, and screening methods)
IT
     Injury
        (traumatic; agents modulating Eph receptor
        activity, therapeutic use, and screening methods)
IT
     14390-96-6, Nitrogen-15, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (42agents modulating Eph receptor activity,
        therapeutic use, and screening methods)
ΙT
     248259-60-1, Ephrin-A8 receptor tyrosine
     kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (EphA8 receptor tyrosine kinase
        ; agents modulating Eph receptor activity,
        therapeutic use, and screening methods)
     7782-41-4, Fluorine-19, biological studies
IT
                                                  12385-13-6, Hydrogen atom,
                        14762-74-4, Carbon-13, biological studies
     biological studies
     142243-02-5, MAP kinase
                              146279-97-2, EphB2
     receptor tyrosine kinase
                               149433-90-9,
     EphB1 receptor tyrosine kinase
     149433-91-0, EphA2 receptor tyrosine
            149433-92-1, Ephrin receptor
     tyrosine kinase
                     160995-45-9, EphA5
     receptor tyrosine kinase
                               167398-03-0,
     EphA4 receptor tyrosine kinase
     204463-92-3, EphA3 receptor tyrosine
              204934-34-9, EphB3 receptor
     tyrosine kinase
                      205132-72-5, EphA7
     receptor tyrosine kinase
                                205132-73-6,
     EphA6 receptor tyrosine kinase
     216974-70-8, EphB4 receptor tyrosine
              225227-27-0, EphB6 receptor
     kinase
```

```
tyrosine kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (agents modulating Eph receptor activity,
        therapeutic use, and screening methods)
IT
     207452-60-6
                   506411-75-2
                                 532441-09-1
                                               532441-10-4
                                                              532441-11-5
     532441-12-6
                   676656-99-8
                                 676657-00-4
                                               676657-01-5
                                                              676657-02-6
                   676657-05-9
     676657-04-8
                                 676657-06-0
                                               676657-07-1
                                                              677716-95-9
     677716-96-0
                   677716-97-1
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     PRP (Properties); BIOL (Biological study)
        (agents modulating Eph receptor activity,
        therapeutic use, and screening methods)
IT
     677716-98-2
                   677716-99-3
                                 677717-00-9
                                               677717-01-0
                                                              677717-02-1
     677717-03-2
                   677717-05-4
                                 677717-06-5
                                               677717-07-6
                                                              677717-08-7
     677717-09-8
                   677717-10-1
                                 677717-11-2
                                               677717-12-3
                                                              677717-13-4
     677717-14-5
                   677717-15-6
                                 677717-16-7
                                               677717-17-8
                                                              677717-18-9
                   677717-20-3
                                 677717-21-4
     677717-19-0
                                               677717-22-5
                                                              677717-23-6
     677717-24-7
                   677717-25-8
                                 677717-26-9
                                               677717-27-0
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (agents modulating Eph receptor activity,
        therapeutic use, and screening methods)
IT
     9001-78-9D, Alkaline phosphatase, ephrin fusion products
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
        (agents modulating Eph receptor activity,
        therapeutic use, and screening methods)
IT
     153369-29-0
                   677716-82-4
                                 677716-83-5
                                               677716-84-6
                                                              677716-85-7
     677716-86-8
                   677716-87-9
                                 677716-88-0
                                               677716-89-1
                                                              677716-90-4
     677716-91-5
                   677716-92-6
                                 677716-93-7
                                               677716-94-8
                                                              677717-28-1
                                 677717-31-6
     677717-29-2
                   677717-30-5
                                               677717-32-7
                                                              677717-33-8
     677717-34-9
                   677717-35-0
     RL: PRP (Properties)
        (unclaimed sequence; agents that modulate Eph
        receptor activity, therapeutic use, and screening methods)
RE.CNT
              THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Mount Sinai Hosptial; WO 0037500 A1 2000 HCAPLUS
     ANSWER 8 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2004:142894 HCAPLUS
DN
     140:180141
ED
     Entered STN: 22 Feb 2004
TI
     EphA2 agonistic monoclonal antibodies for treating epithelial
     cancer, carcinoma and metastasis
IN
     Kinch, Michael S.; Carles-Kinch, Kelly
PA
     Purdue Research Foundation, USA
SO
     PCT Int. Appl., 126 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM A61K
CC
     15-3 (Immunochemistry)
     Section cross-reference(s): 3, 9, 63
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
                                             -----
PΙ
                                            WO 2003-US15046
     WO 2004014292
                         A2
                                20040219
                                                                    20030512 <--
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
```

```
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                20040219
                                          CA 2003-2485548
     CA 2485548
                         AA
                                                                  20030512 <--
                                          US 2003-436783
     US 2004091486
                          A1
                                20040513
                                                                   20030512 <--
PRAI US 2002-379368P
                         Ρ
                                20020510 <--
     US 2002-418204P
                         Ρ
                                20021014 <--
     US 2003-460358P
                         P
                                20030403 <--
     WO 2003-US15046
                         W
                                20030512
CLASS
 PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
 WO 2004014292
                ICM
                        A61K
 WO 2004014292
                ECLA
                        C07K016/24; C07K016/30; C07K016/30B; C07K016/30P
 US 2004091486
                NCL
                        424/155.100
                 ECLA
                        C07K016/30S
     The present invention relates to methods and compns. designed for the
AB
     treatment, management, or prevention of cancer, particularly, metastatic
     cancer. The methods of the invention comprise the administration of an
     effective amount of one or more antibodies that bind to and agonize
     EphA2, thereby increasing EphA2 phosphorylation and
     decreasing EphA2 levels in cells which EphA2 has been
     agonized. The invention also encompasses antibodies that preferentially
     bind an EphA2 epitope exposed on cancer cells but not non-cancer
     cells. The invention also provides pharmaceutical compns. comprising one
     or more EphA2 antibodies of the invention either alone or in
     combination with one or more other agents useful for cancer therapy.
     EphA2 agonist monoclonal antibody hybridoma cancer carcinoma
ST
     metastasis therapy
IT
     Animal cell line
     Antitumor agents
     Bladder, neoplasm
     Blood analysis
     Carcinoma
     Carcinoma
     Chemotherapy
     Drug screening
     Epithelium
     Epitopes
     Genetic vectors
     Human
     Immunotherapy
     Kidney, neoplasm
     Lung, neoplasm
     Mammary gland, neoplasm
     Neoplasm
     Pancreas, neoplasm
     Phosphorylation, biological
     Prostate gland, neoplasm
       Protein sequences
     Radiotherapy
     Skin, neoplasm
     Surgery
     Urine analysis
     cDNA sequences
```

```
(EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     Antibodies and Immunoglobulins
     RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU
     (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties);
     THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study);
     PREP (Preparation); USES (Uses)
        (EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
TΤ
     Nucleic acids
     RL: ARU (Analytical role, unclassified); BSU (Biological study,
     unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     Ligands
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     Hybridoma
        (PTA-4380; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     Hybridoma
        (PTA-4381; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     Blood serum
        (anal.; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
ΙT
     Body fluid
     Needles (tools)
        (aspirates; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
     Health products
        (biologicals; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
        (bladder; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     Diagnosis
        (cancer; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     Bladder, neoplasm
     Lung, neoplasm
     Mammary gland, neoplasm
     Pancreas, neoplasm
     Prostate gland, neoplasm
     Skin, neoplasm
        (carcinoma; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
TΤ
     Drug delivery systems
        (carriers; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IΤ
     Biology
        (cell, host; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
     Intestine, neoplasm
        (colon, carcinoma; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
     Carcinoma
```

```
Intestine, neoplasm
        (colon; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     Carcinoma
        (cutaneous; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
        (enzyme-linked immunosorbent assay; EphA2 agonistic
        monoclonal antibodies for treating epithelial cancer, carcinoma and
        metastasis)
TT
     Tyrosine kinase receptors
     RL: ARU (Analytical role, unclassified); BSU (Biological study,
     unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST
     (Analytical study); BIOL (Biological study); USES (Uses)
        (ephrin type-A receptor
        2; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     Cytometry
        (flow; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     Antibodies and Immunoglobulins
     RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation);
     BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (heavy chain; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
     Antibodies and Immunoglobulins
     RL: ARU (Analytical role, unclassified); BSU (Biological study,
     unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST
     (Analytical study); BIOL (Biological study); USES (Uses)
        (humanized; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
    Diagnosis
        (immunodiagnosis; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
ΙT
     Immunoassay
        (immunofluorescence microscopy; EphA2 agonistic monoclonal
        antibodies for treating epithelial cancer, carcinoma and metastasis)
IT
     Antibodies and Immunoglobulins
     RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation);
     BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (light chain; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
     Carcinoma
        (mammary; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
    Neoplasm
        (metastasis; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
     Antibodies and Immunoglobulins
     RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation);
     BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (monoclonal; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
     Carcinoma
```

```
(pancreatic; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
     Carcinoma
        (prostatic; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
     Carcinoma
        (pulmonary; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
ΙT
     Kidney, neoplasm
        (renal cell carcinoma; EphA2 agonistic monoclonal antibodies
        for treating epithelial cancer, carcinoma and metastasis)
IT
     Carcinoma
        (renal cell; EphA2 agonistic monoclonal antibodies for
        treating epithelial cancer, carcinoma and metastasis)
IT
    Hormones, animal, biological studies
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (therapy; EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     176714-45-7
                   625812-84-2
                                625812-85-3
                                               625812-86-4
                                                             625812-87-5
     625812-88-6
     RL: ARU (Analytical role, unclassified); BSU (Biological study,
     unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic
     use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
        (EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
     149433-91-0, EphA2 receptor tyrosine
TΤ
    kinase
     RL: ARU (Analytical role, unclassified); BSU (Biological study,
     unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST
     (Analytical study); BIOL (Biological study); USES (Uses)
        (EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
     21820-51-9, Phosphotyrosine
TΤ
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (EphA2 agonistic monoclonal antibodies for treating
        epithelial cancer, carcinoma and metastasis)
IT
     660006-49-5P
                    660006-50-8P
     RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation);
     BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (amino acid sequence; EphA2 agonistic monoclonal antibodies
        for treating epithelial cancer, carcinoma and metastasis)
TT
     660006-51-9P
                   660006-52-0P
     RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation);
     BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (nucleotide sequence; EphA2 agonistic monoclonal antibodies
        for treating epithelial cancer, carcinoma and metastasis)
IT
     10540-29-1, Tamoxifen
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (sensitivity enhancement; EphA2 agonistic monoclonal
        antibodies for treating epithelial cancer, carcinoma and metastasis)
                   660007-57-8
                                 660007-58-9 660007-59-0
     660007-56-7
                                                            660007-60-3
     660062-76-0
     RL: PRP (Properties)
        (unclaimed nucleotide sequence; ephA2 agonistic monoclonal
```

antibodies for treating epithelial cancer, carcinoma and metastasis)

```
ANSWER 9 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
ΔN
     2004:98325 HCAPLUS
     140:268510
DN
     Entered STN: 06 Feb 2004
ED
TI
     Inhibition of VEGF-dependent multistage carcinogenesis by
     soluble EphA receptors
     Cheng, Nikki; Brantley, Dana; Fang, Wei Bin; Liu, Hua; Fanslow, William;
AU
     Cerretti, Douglas Pat; Bussell, Katrin N.; Reith, Alastair D.; Jackson,
     Dowdy; Chen, Jin
CS
     Department of Cancer Biology and Vanderbilt-Ingram Cancer Center,
     Vanderbilt University School of Medicine, Nashville, TN, 37232, USA
SO
     Neoplasia (Wilton, CT, United States) (2003), 5(5), 445-456
     CODEN: NEOPFL; ISSN: 1522-8002
PB
     Neoplasia Press Inc.
DT
     Journal
LΑ
     English
CC
     14-1 (Mammalian Pathological Biochemistry)
     Section cross-reference(s): 2
AB
     Elevated expression of Eph receptors has long been
     correlated with the growth of solid tumors. However, the functional role
     of this family of receptor tyrosine kinases
     in carcinogenesis and tumor angiogenesis has not been well characterized.
     Here the authors report that soluble EphA receptors
     inhibit tumor angiogenesis and tumor progression in vivo in the
     RIP-Tag transgenic model of vascular endothelial growth factor
     (VEGF) -dependent multistage pancreatic islet cell carcinoma. Soluble
     EphA receptors delivered either by a transgene or an
     osmotic minipump inhibited the formation of angiogenic islet, a
     premalignant lesion, and reduced tumor volume of solid islet cell carcinoma.
     EphA2-Fc or EphA3-Fc treatment resulted in decreased
     tumor volume but increased tumor and endothelial cell apoptosis in vivo.
     addition, soluble EphA receptors inhibited VEGF
     and BTC tumor cell-conditioned medium-induced endothelial cell
     migration in vitro and VEGF-induced cornea angiogenesis in vivo. A
     dominant neg. EphA2 mutant inhibited, whereas a
     gain-of-function EphA2 mutant enhanced, tumor cell-induced
     endothelial cell migration, suggesting that EphA2
     receptor activation is required for tumor cell-endothelial cell
     interaction. These data provide functional evidence for EphA
     class receptor regulation of VEGF-dependent tumor angiogenesis,
     suggesting that the EphA signaling pathway may represent an
     attractive novel target for antiangiogenic therapy in cancer.
ST
     EphA receptor inhibition VEGF carcinogenesis
     pancreatic islet
     Pancreatic islet of Langerhans, neoplasm
IT
        (carcinoma; soluble EphA receptor inhibition
        of VEGF-dependent multistage pancreatic islet cell carcinogenesis)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor
        2; soluble EphA receptor inhibition
        of VEGF-dependent multistage pancreatic islet cell carcinogenesis)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor 3; soluble RphA
        receptor inhibition of VEGF-dependent multistage
        pancreatic islet cell carcinogenesis)
IT
     Carcinoma
```

```
(pancreatic islet; soluble EphA receptor
        inhibition of VEGF-dependent multistage pancreatic islet cell
        carcinogenesis)
IT
     Transformation, neoplastic
        (soluble EphA receptor inhibition of
        VEGF-dependent multistage pancreatic islet cell carcinogenesis)
IT
     Angiogenesis
     Apoptosis
        (soluble EphA receptor inhibition of
        VEGF-dependent multistage pancreatic islet cell carcinogenesis in
        relation to)
IT
     127464-60-2, Vascular endothelial growth factor
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (soluble EphA receptor inhibition of
        VEGF-dependent multistage pancreatic islet cell carcinogenesis)
RE.CNT
              THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Adams, R; Semin Cell Dev Biol 2002, V13, P55 HCAPLUS
(2) Bargmann, C; Cell 1986, V45, P649 HCAPLUS
(3) Bergers, G; Nat Cell Biol 2000, V2, P737 HCAPLUS
(4) Bergers, G; Science 1999, V284, P808 HCAPLUS
(5) Brantley, D; Oncogene 2002, V21, P7011 HCAPLUS
(6) Cheng, N; Cytokine Growth Factor Rev 2002, V13, P75 HCAPLUS
(7) Coussens, L; Science 2002, V295, P2387 HCAPLUS
(8) Cristofanilli, M; Nat Rev Drug Discov 2002, V1, P415 HCAPLUS
(9) Daniel, T; Cancer Res 1999, V59, P4574 HCAPLUS
(10) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS
(11) Duncan, A; Nature 1988, V332, P563 HCAPLUS
(12) Duncan, A; Nature 1988, V332, P563 HCAPLUS
(13) Flanagan, J; Annu Rev Neurosci 1998, V21, P309 HCAPLUS
(14) Gale, N; Cell Tissue Res 1997, V290, P227 HCAPLUS
(15) Hanahan, D; Cell 1996, V86, P353 HCAPLUS
(16) Hanahan, D; Eur J Cancer 1996, V32A, P2386 HCAPLUS
(17) Hanahan, D; Nature 1985, V315, P115 HCAPLUS
(18) Hattori, M; Science 2000, V289, P1360 HCAPLUS
(19) Holder, N; Development 1999, V126, P2033 HCAPLUS
(20) Jefferis, R; Mol Immunol 1990, V27, P1237 HCAPLUS
(21) Kenyon, B; Invest Ophthalmol Vis Sci 1996, V37, P1625 MEDLINE
(22) Kerbel, R; Nat Rev/Cancer 2002, V2, P727 HCAPLUS
(23) Kisker, O; Cancer Res 2001, V20, P7669
(24) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
(25) Pandey, A; Science 1995, V268, P567 HCAPLUS
(26) Shao, H; J Biol Chem 1995, V270, P5636 HCAPLUS
L40
    ANSWER 10 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2004:60252 HCAPLUS
     140:128427
DN
     Entered STN: 26 Jan 2004
ED
     Preparation of quinazolines as ephrin and EGFR receptor
TΙ
     kinase modulators for treating cancer and other disorders
     Rice, Kenneth D.; Anand, Neel Kumar; Bussenius, Joerg; Costanzo, Simona;
TN
     Kennedy, Abigail R.; Kim, Angie I.; Peto, Csaba J.; Tsang, Tsze H.;
     Blazey, Charles M.
     Exelixis, Inc., USA
PA
SO
     PCT Int. Appl., 266 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM A61K
     28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
CC
```

```
Section cross-reference(s): 1, 33, 63
```

```
FAN.CNT 1
    PATENT NO.
                                                                 DATE
                        KIND DATE
                                          APPLICATION NO.
                                          -----
                       ----
                              -----
     -----
                                                                 -----
    WO 2004006846
                               20040122 WO 2003-US21923
PΙ
                       A2
                                                                 20030714 <--
    WO 2004006846
                        A3
                               20040715
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
            PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
            TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                               20040122 CA 2003-2491191
20050413 EP 2003-764599
                                                               20030714 <--
    CA 2491191
                         AA
    EP 1521747
                         A2
                                                                 20030714 <--
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
                     P
PRAI US 2002-396269P
                               20020715 <--
    US 2003-447212P
                         Ρ
                               20030213 <--
    WO 2003-US21923
                         W
                               20030714
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
WO 2004006846 ICM
                       A61K
WO 2004006846 ECLA
                       C07D239/94; C07D401/12+239+211; C07D401/12+239+213;
                       C07D403/12+239+209; C07D403/12+239+231;
                       C07D405/12+307B+239; C07D405/12+319+239;
                       C07D413/12+265D+239; C07D413/12+271+239;
                       C07D417/12+277B+239; C07D451/06C;
                       C07D471/04+221A+221AC07D403/12+239+209;
                       C07D487/04+241C+209C; C07D487/04+241C+221C;
                       C07D493/04+307B+307B+2; C07D498/04+265C+209C;
                       C07D498/04+265C+265C+2
os
    MARPAT 140:128427
GI
```

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides quinazolines (shown as I; variables defined below; e.g. II and III) for modulating receptor tyrosine kinase activity, particularly ephrin and EGFR, and methods of treating diseases mediated by receptor kinase activity using the compds. and pharmaceutical compns. thereof. Diseases mediated by receptor kinase activity include, but are not limited to, diseases characterized in part by abnormal levels of cell proliferation (i.e. tumor growth), programmed cell death (apoptosis), cell migration and invasion and angiogenesis associated with tumor growth. Compds. of the invention include 'spectrum selective' kinase modulators, compds. that inhibit, regulate and/or modulate signal transduction across subfamilies of receptor-type tyrosine kinases, including ephrin and EGFR. Inhibitory activities for >200 examples of I are tabulated for some or all of EphB4, EphA2, KDR, Flt-1, EGFR and ErbB2 kinases. Although the methods of preparation are not claimed,

37 example prepns. are included. For example, 1,4:3,6-dianhydro-2-0-[4-[(3-chloro-2-methylphenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-0-methyl-L-iditol hydrochloride was prepared in 2 steps (94, 51 % yields, resp.) starting with mesylation of 1,4:3,6-dianhydro-2-0-methyl-D-glucitol followed by ether formation of the intermediate 1,4:3,6-dianhydro-2-0methyl-5-0-(methylsulfonyl)-D-glucitol with 4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-ol; the quinazolinol was prepared in 64 % yield from 4-chloro-6-(methyloxy)-7-[(phenylmethyl)oxy]quinazoline hydrochloride and 3,4-dichloroaniline. For I: R1 is C1-C3 (un)substituted alkyl; R2 = H, halogen, trihalomethyl, CN, NH2, NO2, OR3, N(R3)R4, S(O)0-2R4, SO2N(R3)R4, CO2R3, C(O)N(R3)R4, N(R3)SO2R4, N(R3)C(O)R3, N(R3)CO2R4, C(0)R3, (un)substituted lower alkyl, (un)substituted lower alkenyl, and (un) substituted lower alkynyl; R3 is H or R4; R4 = (un) substituted lower alkyl, (un) substituted aryl, (un) substituted lower arylalkyl, (un) substituted heterocyclyl, and (un) substituted lower heterocyclylalkyl; or R3 and R4, when taken together with a common N to which they are attached, form an (un) substituted 5-7-membered heterocyclyl, said (un) substituted five-to seven-membered heterocyclyl optionally containing at least one addnl. heteroatom = N, O, S, and P. Q is 0-5; Z = OCH2, O, S(0)0-2, N(R5)CH2, and NR5; R5 is -H or (un)substituted lower alkyl; M1 is H, (un) substituted C1-C8 alkyl-L2-L1, G(CH2)0-3, or R53(R54)N(CH2)0-3; wherein G is a saturated 5-7-membered heterocyclyl containing 1-2 annular heteroatoms; L1 is C:O or SO2; L2 is a direct bond, O, or NH; M2 is a saturated or mono- or polyunsatd. C3-C14 mono- or fused-polycyclic hydrocarbyl optionally containing 1-3 annular heteroatoms per ring; M3 is NR9, O, or absent; M4 is CH2, CH2CH2, CH2CH2CH2, or absent; addnl. details are given in the claims. quinazoline prepn ephrin EGFR receptor kinase

ST inhibitor antitumor compn

IT Alditols

> RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(drug candidate; preparation of quinazolines as ephrin and EGFR receptor kinase modulators for treating cancer and other disorders)

IT Antitumor agents

Apoptosis

Drug delivery systems

Human

Neoplasm

(preparation of quinazolines as ephrin and EGFR receptor kinase modulators for treating cancer and other disorders)

IT Structure-activity relationship

(protein (tyrosine) kinase-

inhibiting; preparation of quinazolines as ephrin and EGFR receptor kinase modulators for treating cancer and other disorders)

IT Vascular endothelial growth factor receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (type VEGFR-2, inhibitors; preparation of quinazolines as ephrin and EGFR receptor kinase modulators

for treating cancer and other disorders)

IT 650577-72-3P 650579-40-1P 650579-56-9P 650579-55-8P 650579-73-0P 650579-75-2P 650579-79-6P 650579-84-3P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(drug candidate; preparation of quinazolines as ephrin and EGFR receptor kinase modulators for treating cancer and

```
other disorders)
IT
     650577-29-0P
                     650577-32-5P
                                    650577-33-6P
                                                    650577-34-7P
                                                                    650577-35-8P
     650577-36-9P
                     650577-37-0P
                                    650577-38-1P
                                                    650577-39-2P
                                                                    650577-40-5P
     650577-41-6P
                     650577-42-7P
                                    650577-43-8P
                                                    650577-44-9P
                                                                    650577-45-0P
     650577-46-1P
                     650577-47-2P
                                    650577-48-3P
                                                    650577-53-0P
                                                                    650577-57-4P
     650577-64-3P
                     650577-69-8P
                                    650577-73-4P
                                                    650577-74-5P
                                                                    650577-75-6P
     650577-76-7P
                     650577-79-0P
                                    650577-80-3P
                                                    650577-81-4P
                                                                    650577-82-5P
                                                                    650577-92-7P
     650577-83-6P
                     650577-89-2P
                                    650577-90-5P
                                                    650577-91-6P
     650577-93-8P
                     650577-96-1P
                                    650578-03-3P
                                                    650578-07-7P
                                                                    650578-08-8P
     650578-09-9P
                     650578-10-2P
                                    650578-11-3P
                                                    650578-18-0P
                                                                    650578-19-1P
     650578-20-4P
                     650578-23-7P
                                    650578-24-8P
                                                    650578-25-9P
                                                                    650578-26-0P
     650578-28-2P
                     650578-29-3P
                                    650578-30-6P
                                                    650578-31-7P
                                                                    650578-32-8P
     650578-33-9P
                     650578-34-0P
                                    650578-35-1P
                                                    650578-36-2P
                                                                    650578-41-9P
     650578-50-0P
                     650578-51-1P
                                    650578-52-2P
                                                    650578-53-3P
                                                                    650578-54-4P
     650578-55-5P
                     650578-56-6P
                                    650578-57-7P
                                                    650578-58-8P
                                                                    650578-59-9P
     650578-60-2P
                     650578-61-3P
                                    650578-62-4P
                                                    650578-64-6P
                                                                    650578-65-7P
                                    650578-75-9P
     650578-68-0P
                     650578-70-4P
                                                    650578-83-9P
                                                                    650578-84-0P
     650578-85-1P
                     650578-86-2P
                                    650578-87-3P
                                                    650578-88-4P
                                                                    650578-89-5P
     650578-90-8P
                     650578-91-9P
                                    650578-92-0P
                                                    650578-93-1P
                                                                    650578-94-2P
     650578-95-3P
                     650578-96-4P
                                    650578-97-5P
                                                    650578-98-6P
                                                                    650578-99-7P
                                    650579-02-5P
     650579-00-3P
                     650579-01-4P
                                                    650579-03-6P
                                                                    650579-04-7P
                                    650579-07-0P
     650579-05-8P
                     650579-06-9P
                                                    650579-08-1P
                                                                    650579-09-2P
     650579-10-5P
                     650579-11-6P
                                    650579-12-7P
                                                    650579-13-8P
                                                                    650579-14-9P
     650579-15-0P
                     650579-16-1P
                                    650579-17-2P
                                                    650579-18-3P
                                                                    650579-19-4P
     650579-20-7P
                     650579-21-8P
                                    650579-22-9P
                                                    650579-23-0P
                                                                    650579-24-1P
     650579-25-2P
                     650579-26-3P
                                    650579-27-4P
                                                    650579-28-5P
                                                                    650579-29-6P
     650579-30-9P
                     650579-31-0P
                                    650579-32-1P
                                                    650579-33-2P
                                                                    650579-34-3P
     650579-35-4P
                     650579-36-5P
                                    650579-37-6P
                                                    650579-41-2P
                                                                    650579-42-3P
     650579-43-4P
                     650579-44-5P
                                                    650579-46-7P
                                    650579-45-6P
                                                                    650579-48-9P
     650579-50-3P
                     650579-52-5P
                                    650579-57-0P
                                                    650579-58-1P
                                                                    650579-59-2P
     650579-60-5P
                     650579-61-6P
                                    650579-62-7P
                                                    650579-64-9P
                                                                    650579-67-2P
     650579-68-3P
                     650579-69-4P
                                    650579-76-3P
                                                    650579-77-4P
                                                                    650579-80-9P
                     650579-85-4P
     650579-81-0P
                                    650579-86-5P
                                                    650579-87-6P
                                                                    650579-88-7P
     650579-89-8P
                     650579-90-1P
                                    650579-91-2P
                                                    650579-92-3P
                                                                    650579-93-4P
                                    650579-96-7P
     650579-94-5P
                     650579-95-6P
                                                    650579-97-8P
                                                                    650579-98-9P
     650579-99-0P
                     650580-00-0P
                                    650580-01-1P
                                                    650580-02-2P
                                                                    650580-03-3P
     650580-04-4P
                     650580-05-5P
                                    650580-06-6P
                                                    650580-07-7P
                                                                    650580-08-8P
     650580-09-9P
                     650580-10-2P
                                    650580-11-3P
                                                    650580-12-4P
                                                                    650580-13-5P
     650580-14-6P
                     650580-15-7P
                                    650580-16-8P
                                                    650580-17-9P
                                                                    650580-18-0P
     650580-19-1P
                     650580-20-4P
                                    650580-21-5P
                                                    650580-22-6P
                                                                    650580-23-7P
     650580-24-8P
                     650580-25-9P
                                    650580-26-0P
                                                    650580-27-1P
                                                                    650580-28-2P
     650580-29-3P
                     650580-30-6P
                                    650580-31-7P
                                                    650580-32-8P
                                                                    650580-33-9P
     650580-34-0P
                     650580-35-1P
                                    650580-36-2P
                                                    650580-37-3P
                                                                    650580-38-4P
     650580-39-5P
                     650580-40-8P
                                    650580-41-9P
                                                    650580-42-0P
                                                                    650580-43-1P
     650580-44-2P
                     650580-45-3P
                                    650580-46-4P
                                                    650580-47-5P
                                                                    650580-48-6P
     650580-49-7P
                     650580-50-0P
                                    650580-51-1P
                                                    650580-52-2P
                                                                    650580-53-3P
     650580-54-4P
                     650580-55-5P
                                    650580-56-6P
                                                    650580-57-7P
                                                                    650580-58-8P
     650580-59-9P
                     650580-60-2P
                                    650580-61-3P
                                                    650580-62-4P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (drug candidate; preparation of quinazolines as ephrin and EGFR
        receptor kinase modulators for treating cancer and
        other disorders)
IT
     650580-63-5P
                     650580-64-6P
                                    650580-65-7P
                                                    650580-66-8P
                                                                    650580-67-9P
     650580-68-0P
                     650580-69-1P
                                    650580-70-4P
                                                    650580-71-5P
                                                                    650580-72-6P
     650580-73-7P
                     650580-74-8P
                                    650580-75-9P
                                                    650580-76-0P
                                                                    650580-77-1P
     650580-78-2P
                     650580-79-3P
                                    650580-80-6P
                                                    650580-81-7P
                                                                    650580-82-8P
     650580-83-9P
                     650580-84-0P
                                    650580-85-1P
                                                    650580-86-2P
                                                                    650580-87-3P
     650580-88-4P
                     650580-89-5P
                                    650580-90-8P
                                                    650580-91-9P
                                                                    650580-92-0P
```

```
650580-93-1P
               650580-94-2P
                               650580-95-3P
                                               650580-96-4P
                                                               650580-97-5P
650580-98-6P
               650580-99-7P
                               650581-00-3P
                                               650581-01-4P
                                                               650581-02-5P
650581-03-6P
               650581-04-7P
                               650581-05-8P
                                               650581-06-9P
                                                               650581-07-0P
650581-08-1P
               650581-09-2P
                               650581-10-5P
                                               650581-11-6P
                                                               650581-12-7P
650581-13-8P
               650581-14-9P
                               650581-15-0P
                                               650581-16-1P
                                                               650581-17-2P
650581-18-3P
               650581-19-4P
                               650581-20-7P
                                               650581-21-8P
                                                               650581-22-9P
650581-23-0P
               650581-24-1P
                               650581-25-2P
                                               650581-26-3P
                                                               650581-27-4P
650581-28-5P
               650581-29-6P
                               650581-30-9P
                                               650581-31-0P
                                                               650581-32-1P
               650581-34-3P
                               650581-35-4P
                                               650581-36-5P
650581-33-2P
                                                               650581-37-6P
               650581-39-8P
                                               650581-41-2P
                               650581-40-1P
650581-38-7P
                                                               650581-42-3P
650581-43-4P
               650581-44-5P
                               650581-45-6P
                                               650581-46-7P
                                                               650581-47-8P
                                               650581-51-4P
650581-48-9P
               650581-49-0P
                               650581-50-3P
                                                               650581-52-5P
               650581-54-7P
650581-53-6P
                               650581-55-8P
                                               650581-56-9P
                                                               650581-57-0P
                                               650581-61-6P
650581-58-1P
               650581-59-2P
                               650581-60-5P
                                                               650581-62-7P
                               650581-65-0P
650581-63-8P
               650581-64-9P
                                               650581-66-1P
                                                               650581-67-2P
                               650581-70-7P
650581-68-3P
               650581-69-4P
                                               650581-71-8P
                                                               650581-72-9P
                               650581-75-2P
                                               650581-76-3P
650581-73-0P
               650581-74-1P
                                                               650581-77-4P
650581-78-5P
               650581-79-6P
                               650581-80-9P
                                               650581-81-0P
                                                               650581-82-1P
                                               650581-86-5P
650581-83-2P
               650581-84-3P
                               650581-85-4P
                                                               650581-87-6P
                               650581-90-1P
                                               650581-91-2P
650581-88-7P
               650581-89-8P
                                                               650581-92-3P
                                               650581-96-7P
650581-93-4P
               650581-94-5P
                               650581-95-6P
                                                               650581-97-8P
                               650582-00-6P
                                               650582-01-7P
650581-98-9P
               650581-99-0P
                                                               650582-02-8P
650582-03-9P
               650582-04-0P
                               650582-05-1P
                                               650582-06-2P
                                                               650582-07-3P
                                                               650582-12-0P
650582-08-4P
               650582-09-5P
                               650582-10-8P
                                               650582-11-9P
650582-13-1P
               650582-14-2P
                               650582-15-3P
                                               650582-16-4P
                                                               650582-17-5P
                                                               650582-22-2P
650582-18-6P
               650582-19-7P
                               650582-20-0P
                                               650582-21-1P
                                                               650582-27-7P
650582-23-3P
               650582-24-4P
                               650582-25-5P
                                               650582-26-6P
                               650582-30-2P
650582-28-8P
               650582-29-9P
                                               650582-31-3P
                                                               650582-32-4P
               650582-34-6P
                               650582-35-7P
                                               650582-36-8P
650582-33-5P
                                                               650582-37-9P
650582-38-0P
               650582-39-1P
                               650582-40-4P
                                               650582-41-5P
                                                               650582-42-6P
                               650582-45-9P
                                               650582-46-0P
                                                               650582-47-1P
650582-43-7P
               650582-44-8P
                               650582-50-6P
               650582-49-3P
650582-48-2P
                                               650582-51-7P
                                                               650582-52-8P
               650582-54-0P
                                                               650582-57-3P
650582-53-9P
                               650582-55-1P
                                               650582-56-2P
                                               650582-61-9P
650582-58-4P
               650582-59-5P
                               650582-60-8P
                                                               650582-62-0P
                                               650582-66-4P
                               650582-65-3P
650582-63-1P
               650582-64-2P
                                                               650582-67-5P
               650582-69-7P
                               650582-70-0P
                                               650582-71-1P
                                                               650582-72-2P
650582-68-6P
650582-73-3P
               650582-74-4P
                               650582-75-5P
                                               650582-76-6P
                                                               650582-77-7P
650582-78-8P
               650582-79-9P
                               650582-80-2P
                                               650582-81-3P
                                                               650582-82-4P
                                                               650582-87-9P
650582-83-5P
               650582-84-6P
                               650582-85-7P
                                               650582-86-8P
650582-88-0P
               650582-89-1P
                               650582-90-4P
                                               650582-91-5P
                                                               650582-92-6P
650582-93-7P
               650582-94-8P
                               650582-95-9P
                                               650582-96-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
```

(drug candidate; preparation of quinazolines as **ephrin** and EGFR **receptor kinase** modulators for treating cancer and other disorders)

```
IT
     650582-97-1P
                     650582-98-2P
                                     650582-99-3P
                                                     650583-00-9P
                                                                     650583-01-0P
     650583-02-1P
                                                    650583-05-4P
                     650583-03-2P
                                     650583-04-3P
                                                                     650583-06-5P
                     650583-08-7P
                                                     650583-10-1P
     650583-07-6P
                                     650583-09-8P
                                                                     650583-11-2P
     650583-12-3P
                     650583-13-4P
                                     650583-14-5P
                                                     650583-15-6P
                                                                     650583-16-7P
     650583-17-8P
                     650583-18-9P
                                     650583-19-0P
                                                     650583-20-3P
                                                                     650583-21-4P
     650583-22-5P
                     650583-23-6P
                                     650583-24-7P
                                                    650583-25-8P
                                                                     650583-26-9P
     650583-27-0P
                     650583-28-1P
                                     650583-29-2P
                                                    650583-30-5P
                                                                     650583-31-6P
     650583-32-7P
                     650583-33-8P
                                     650583-34-9P
                                                     650583-35-0P
                                                                     650583-36-1P
     650583-37-2P
                     650583-38-3P
                                     650583-39-4P
                                                     650583-40-7P
                                                                     650583-41-8P
     650583-42-9P
                     650583-43-0P
                                     650583-44-1P
                                                     650583-45-2P
                                                                     650583-46-3P
     650583-47-4P
                     650583-48-5P
                                     650583-49-6P
                                                     650583-50-9P
                                                                     650583-51-0P
     650583-52-1P
                     650583-53-2P
                                     650583-54-3P
                                                     650583-55-4P
                                                                     650583-56-5P
                                     650583-59-8P
     650583-57-6P
                     650583-58-7P
                                                     650583-60-1P
                                                                    650583-61-2P
```

```
650583-62-3P
                    651031-01-5P
                                   651031-02-6P
                                                  651031-03-7P
                                                                 651031-04-8P
     651031-05-9P
                    651031-06-0P
                                   651031-07-1P
                                                  651031-08-2P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (drug candidate; preparation of quinazolines as ephrin and EGFR
        receptor kinase modulators for treating cancer and
        other disorders)
     79079-06-4, EGFR tyrosine kinase
TT
                                        108891-60-7, FMS
     receptor tyrosine kinase 137632-09-8, ErbB2
     tyrosine kinase 149433-91-0, EphA2
     receptor tyrosine kinase 216974-70-8,
     EphB4 receptor tyrosine kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors; preparation of quinazolines as ephrin and
        EGFR receptor kinase modulators for treating cancer
        and other disorders)
IT
     65-85-0, Benzoic acid, reactions
                                        95-76-1, 3,4-Dichloroaniline
                                                                       96-32-2,
     Methyl bromoacetate 106-89-8, Epichlorohydrin, reactions
                                                                 532-24-1,
     8-Methyl-8-azabicyclo[3.2.1]octan-3-one 534-07-6, 1,3-Dichloroacetone
                                         563-79-1, 2,3-Dimethylbut-2-ene
     541-41-3, Ethyl chloridocarbonate
     874-77-1 926-64-7, (Dimethylamino)acetonitrile 2133-40-6, L-Proline
     methyl ester hydrochloride
                                  3943-74-6, Methyl vanillate
                                                                5807-02-3,
     4-Morpholineacetonitrile 6941-54-4 13831-31-7, Acetoxyacetyl chloride
                 23356-96-9, (S)-(+)-Prolinol
     16684-31-4
                                                 24808-23-9
                                                              35130-97-3
     39684-80-5, 1,1-Dimethylethyl (2-bromoethyl)carbamate
                                                             40987-25-5,
     2-(Chloromethyl)-4-(phenylmethyl)morpholine 57260-71-6,
     1,1-Dimethylethyl 1-piperazinecarboxylate
                                                 76211-05-7
                                                              84358-13-4
     99380-85-5
                  112018-06-1 139228-12-9
                                              146231-54-1
                                                            157904-95-5
                   193001-44-4
     188869-05-8
                                 211053-49-5
                                               214834-18-1
                                                             273207-59-3
                                 650577-63-2
                   650577-55-2
     650577-52-9
                                               650577-78-9
                                                             650577-88-1
     650577-95-0
                   650578-16-8
                                 650578-27-1
                                               650578-39-5
                                                             650578-49-7
     650578-72-6
                   650578-82-8
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of quinazolines as ephrin and EGFR receptor
        kinase modulators for treating cancer and other disorders)
IT
     939-56-0P, Cyanomethyl benzoate
                                       16888-43-0P, 4-Morpholineethanethioamide
     27203-18-5P
                   27507-28-4P
                                 113534-02-4P
                                                122894-70-6P,
     2-(Chloromethyl)morpholine
                                 137499-44-6P
                                                 164926-91-4P
                                                                194151-77-4P
     650577-30-3P
                                   650577-49-4P
                    650577-31-4P
                                                  650577-50-7P
                                                                 650577-51-8P
     650577-54-1P
                    650577-56-3P
                                   650577-58-5P
                                                  650577-59-6P
                                                                 650577-60-9P
     650577-61-0P
                    650577-62-1P
                                   650577-65-4P
                                                  650577-66-5P
                                                                 650577-67-6P
     650577-68-7P
                    650577-70-1P
                                   650577-71-2P
                                                  650577-84-7P
                                                                 650577-85-8P
     650577-86-9P
                    650577-94-9P
                                   650577-97-2P
                                                  650577-98-3P
                                                                 650577-99-4P
     650578-00-0P
                    650578-01-1P
                                   650578-02-2P
                                                  650578-04-4P
                                                                 650578-05-5P
     650578-06-6P
                    650578-12-4P
                                   650578-13-5P
                                                  650578-14-6P
                                                                 650578-17-9P
     650578-21-5P
                    650578-22-6P
                                   650578-37-3P
                                                  650578-38-4P
                                                                 650578-40-8P
     650578-42-0P
                    650578-43-1P
                                   650578-44-2P
                                                  650578-45-3P
                                                                 650578-46-4P
     650578-47-5P
                    650578-48-6P
                                   650578-63-5P
                                                  650578-66-8P
                                                                 650578-69-1P
     650578-71-5P
                    650578-73-7P
                                   650578-74-8P
                                                  650578-76-0P
                                                                 650578-77-1P
     650578-78-2P
                    650578-79-3P
                                   650578-80-6P
                                                  650578-81-7P
                                                                 650579-38-7P
     650579-39-8P
                    650579-47-8P
                                   650579-49-0P
                                                  650579-51-4P
                                                                 650579-53-6P
     650579-54-7P
                    650579-63-8P
                                                  650579-66-1P
                                   650579-65-0P
                                                                 650579-70-7P
     650579-71-8P
                    650579-72-9P
                                   650579-74-1P
                                                  650579-78-5P
                                                                 650579-82-1P
     650579-83-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of quinazolines as ephrin and EGFR receptor
        kinase modulators for treating cancer and other disorders)
```

```
L40 ANSWER 11 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2004:8305 HCAPLUS
DN
     140:160837
     Entered STN: 07 Jan 2004
ED
     Proto-oncogene c-Cbl promotes the degradation of EphA2
ΤI
     receptor tyrosine kinase
ΑU
     Wang, You-jie; Li, Zhong-you; Lu, Bin; Zou, Li-jun; Zhou, Yi-kai;
     Sugimura, Haruhiko
     Institute of Environmental Medicine, Tangji Medical College, Huazhong
CS
     University of Science & Technology, Wuhan, 430030, Peop. Rep. China
     Zhongquo Shengwu Huaxue Yu Fenzi Shengwu Xuebao (2003), 19(6),
SO
     785-790
     CODEN: ZSHXF2; ISSN: 1007-7626
     Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao Bianweihui
PB
DT
     Journal
LA
     Chinese
CC
     13-2 (Mammalian Biochemistry)
AB
     The product of proto-oncogene c-Cbl has been proved as a new ubiquitin
     ligase (E3) of RING finger type for ubiquitin-proteasome pathway. Some
     studies reported that c-Cbl exerted the neg. regulation to
     receptor tyrosine kinases and non-
     receptor tyrosine kinases by promoting their
     degradation Eph receptor is the largest subfamily of
     receptor tyrosine kinase, but understanding of
     the activity regulation to this subfamily is quite poor. It has been
     demonstrated in our previous study that c-Cbl could neg. regulate the
     activity of EphA2 with an unknown mechanism. In this
     communication, it was shown that c-Cbl mediated degradation of EphA2
     after it was activated by the ligand binding. It was also shown that
     EphA2 was rapidly degraded in response to the ligand stimulation,
     and this degradation could be blocked by MG132, an inhibitor
     of proteasome activity. Based on this result, it was proposed that c-Cbl
     might serve as E3 to mediate the ubiquitination of EphA2 and
     promoted its degradation in proteasome.
ST
     proto oncogene cCbl EphA2 receptor tyrosine
     kinase proteasome
IT
     Gene, animal
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (oncogene, c-Cbl; proto-oncogene c-Cbl promotes degradation of
        EphA2 receptor tyrosine kinase in
        proteasome after it is activated by ligand binding)
TΤ
    Human
       Protein degradation
        (proto-oncogene c-Cbl promotes degradation of EphA2
        receptor tyrosine kinase in proteasome
        after it is activated by ligand binding)
TT
     140879-24-9, Proteasome 149433-91-0, EphA2
     receptor tyrosine kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (proto-oncogene c-Cbl promotes degradation of EphA2
        receptor tyrosine kinase in proteasome
        after it is activated by ligand binding)
L40 ANSWER 12 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
ΔN
     2004:7663 HCAPLUS
DN
     140:197154
ED
    Entered STN: 06 Jan 2004
    Ligand Binding Up-Regulates EphA2 Messenger RNA Through the
TΙ
     Mitogen-Activated Protein/Extracellular Signal-Regulated
     Kinase Pathway
```

haddad - 10 / 823259 ΑU Pratt, Rebecca L.; Kinch, Michael S. CS Department of Basic Medical Sciences, Purdue University Cancer Center, West Lafayette, IN, USA Molecular Cancer Research (2003), 1(14), 1070-1076 SO CODEN: MCROC5; ISSN: 1541-7786 PB American Association for Cancer Research DTJournal English LA CC 14-1 (Mammalian Pathological Biochemistry) AB The EphA2 receptor tyrosine kinase is overexpressed in aggressive cancer cells, where it critically influences many aspects of malignant character. Although high levels of EphA2 have been documented in many different cancers, relatively little is known of the mechanisms that govern EphA2 gene expression in normal or malignant cells. Our present studies demonstrate that EphA2 influences the regulation of its own gene expression. Specifically, ligand-mediated phosphorylation of EphA2 transmits signals to the nucleus via extracellular signal-regulated kinase kinases to up-regulate de novo EphA2 gene expression and synthesis. This mechanism governs EphA2 expression in normal and malignant cells. In normal cells, EphA2 protein expression is balanced by ligand-mediated induction of EphA2 gene expression countered by EphA2 protein turnover. These findings suggest that EphA2 expression and ligand binding are intimately linked in epithelial cells. Increased understanding of this mechanism could have important implications for understanding the causes of EphA2 overexpression and for developing new strategies for therapeutic intervention in the many cancers that overexpress EphA2. ligand binding upregulate EphA2 mRNA ERK kinase breast ST cancer IΤ Epithelium

(${\tt EphA2}$ expression and ligand binding are intimately linked in epithelial cells)

IT Gene, animal

mRNA

RL: BSU (Biological study, unclassified); BIOL (Biological study) (EphA2; ligand binding up-regulates EphA2 mRNA through the mitogen-activated protein/extracellular signal-regulated kinase pathway in MDA-MB-231 cell line)

IT Ligands

RL: BSU (Biological study, unclassified); BIOL (Biological study) (binding; ligand binding up-regulates EphA2 mRNA through the mitogen-activated protein/extracellular signal-regulated kinase pathway in MDA-MB-231 cell line)

IT Tyrosine kinase receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (ephrin type-A receptor

2; In normal cells, EphA2 protein
expression is balanced by ligand-mediated induction of EphA2
gene expression countered by EphA2 protein
turnover)

IT Mammary gland, neoplasm

(human MDA-MB-231 cell line; ligand binding up-regulates **EphA2** mRNA through the mitogen-activated **protein**/extracellular signal-regulated **kinase** pathway in MDA-MB-231 cell line)

IT Human

(ligand binding up-regulates **EphA2** mRNA through the mitogen-activated **protein**/extracellular signal-regulated **kinase** pathway in MDA-MB-231 cell line)

```
IT
     Cell nucleus
     Signal transduction, biological
        (ligand-mediated phosphorylation of EphA2 transmits signals
        to the nucleus via extracellular signal-regulated kinase
        kinases to up-regulate de novo EphA2 gene expression
        and synthesis)
IT
     Phosphorylation, biological
        (protein; ligand-mediated phosphorylation of EphA2
        transmits signals to the nucleus via extracellular signal-regulated
        kinase kinases to up-regulate de novo EphA2
        gene expression and synthesis)
     142243-02-5, Extracellular signal-regulated kinase
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ligand binding up-regulates EphA2 mRNA through the
        mitogen-activated protein/extracellular signal-regulated
        kinase pathway in MDA-MB-231 cell line)
              THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RE
(1) Andres, A; Int J Cancer 1995, V63, P288 HCAPLUS
(2) Andres, A; Oncogene 1994, V9, P1461 HCAPLUS
(3) Ben-Ze'Ev, A; Adv Exp Med Biol 1994, V358, P147 HCAPLUS
(4) Berx, G; Breast Cancer Res 2001, V3, P289 HCAPLUS
(5) Biervert, C; Neurosci Lett 2001, V315, P25 HCAPLUS
(6) Brantley, D; Oncogene 2002, V21, P7011 HCAPLUS
(7) Carles-Kinch, K; Cancer Res 2002, V62, P2840 HCAPLUS
(8) Cheng, N; Mol Cancer Res 2002, V1, P2 HCAPLUS
(9) Cox, A; Cancer Biol Ther 2002, V1, P599 HCAPLUS
(10) Davis, S; Science 1994, V266, P816 HCAPLUS
(11) Dohn, M; Oncogene 2001, V20, P6503 HCAPLUS
(12) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
(13) Elowe, S; Mol Cell Biol 2001, V21, P7429 HCAPLUS
(14) Hajra, K; Genes Chromosomes & Cancer 2002, V34, P255 HCAPLUS
(15) Kataoka, H; J Cancer Res Clin Oncol 2002, V128, P343 HCAPLUS
(16) Katzenellenbogen, B; Biol Reprod 1996, V54, P287 HCAPLUS
(17) Kinch, M; Clin Cancer Res 2003, V9, P613 HCAPLUS
(18) Koolpe, M; J Biol Chem 2002, V277, P46974 HCAPLUS
(19) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
(20) Liu, W; Cancer 2002, V94, P934 HCAPLUS
(21) Mareel, M; Physiol Rev 2003, V83, P337 HCAPLUS
(22) McCormick, F; Curr Opin Biotechnol 1996, V7, P449 HCAPLUS
(23) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
(24) Miao, H; Nat Cell Biol 2001, V3, P527 HCAPLUS
(25) Miyazaki, T; Int J Cancer 2003, V103, P657 HCAPLUS
(26) Ogata, H; Cancer Lett 2001, V172, P159 HCAPLUS
(27) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
(28) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS
(29) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS
(30) Pandey, A; Science 1995, V268, P567 HCAPLUS
(31) Potla, L; Cancer Lett 2002, V175, P187 HCAPLUS
(32) Pratt, R; Oncogene 2002, V21, P7690 HCAPLUS
(33) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
(34) Shapiro, P; Crit Rev Clin Lab Sci 2002, V39, P285 HCAPLUS
(35) Sherr, C; Cancer Cell 2002, V2, P103 HCAPLUS
(36) Tong, J; J Biol Chem 2003, V278, P6111 HCAPLUS
(37) Walker-Daniels, J; Mol Cancer Res 2002, V1, P79 HCAPLUS
(38) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
(39) Yamada, K; Curr Opin Cell Biol 1997, V9, P76 HCAPLUS
```

(40) Zantek, N; Cell Growth & Differ 1999, V10, P629 HCAPLUS

- (41) Zantek, N; Clin Cancer Res 2001, V7, P3640 HCAPLUS
- (42) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
- (43) Zelinski, D; J Cell Biochem 2002, V85, P714 HCAPLUS
- (44) Zschiesche, W; Anticancer Res 1997, V17, P561 MEDLINE
- L40 ANSWER 13 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2004:4755 HCAPLUS
- DN 140:143672
- ED Entered STN: 05 Jan 2004
- TI High-level expression of EphA2 receptor tyrosine kinase in prostatic intraepithelial neoplasia
- AU Zeng, Guangyuan; Hu, Zhiqiang; Kinch, Michael S.; Pan, Chong-Xian; Flockhart, David A.; Kao, Chinghai; Gardner, Thomas A.; Zhang, Shaobo; Li, Lang; Baldridge, Lee Ann; Koch, Michael O.; Ulbright, Thomas M.; Eble, John N.; Cheng, Liang
- CS Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis, IN, USA
- SO American Journal of Pathology (2003), 163(6), 2271-2276 CODEN: AJPAA4; ISSN: 0002-9440
- PB American Society for Investigative Pathology
- DT Journal
- LA English
- CC 14-1 (Mammalian Pathological Biochemistry)
 AB EphA2 is a transmembrane receptor tyrosine
 - EphA2 is a transmembrane receptor tyrosine kinase that is overexpressed in many carcinomas. Specific targeting of EphA2 with monoclonal antibodies is sufficient to inhibit the growth, migration and invasiveness of aggressive cancers in animal models. Using immunohistochem. analyses, the authors measured the expression of EphA2 in prostatic adenocarcinoma, high-grade prostatic intraepithelial neoplasia, and adjacent benign prostate tissue from 93 radical prostatectomy specimens. These results were related to multiple clin. and pathol. characteristics. The fraction of cells staining pos. with EphA2 in benign prostatic epithelium (mean, 12%) was significantly lower than that in high-grade prostatic intraepithelial neoplasia (mean, 67%, P < 0.001) and prostatic adenocarcinoma (mean, 85%, P < 0.001). Moreover, the intensity of EphA2 immunoreactivity in prostatic adenocarcinoma was significantly higher than in benign prostatic tissue (P < 0.001) or high-grade prostatic intraepithelial neoplasia (P < 0.001). Benign prostatic epithelium showed weak or no immunoreactivity for EphA2 in all cases examined Whereas EphA2 immunoreactivity related to neoplastic transformation, it did not correlate with other clin. and pathol. parameters examined These data suggest that EphA2 levels increase as prostatic epithelial cells progress toward a more aggressive phenotype. Progressively higher levels of EphA2 in high-grade prostatic intraepithelial neoplasia and prostatic carcinoma are consistent with recent evidence that EphA2 functions as a powerful oncogene. Moreover, the presence of high levels of EphA2 in these cells suggests opportunities for prostate cancer prevention and treatment.
- ST EphA2 receptor tyrosine kinase prostate neoplastic transformation; prostate intraepithelial neoplasia EphA2 receptor tyrosine kinase

 IT Human
 - (EphA2 receptor Tyr kinase overexpression in prostatic intraepithelial neoplasia)
- IT Prostate gland, neoplasm
 - (adenocarcinoma; EphA2 receptor Tyr kinase
 - overexpression in prostatic neoplastic transformation)
- IT Prostate gland, disease

```
(benign hyperplasia; EphA2 receptor Tyr
        kinase overexpression in prostatic neoplastic transformation)
IT
     Hyperplasia
        (benign prostatic; EphA2 receptor Tyr
        kinase overexpression in prostatic neoplastic transformation)
IT
     Gene, animal
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (eck protein; EphA2 receptor
        Tyr kinase overexpression in prostatic intraepithelial
        neoplasia)
IT
     Prostate gland, neoplasm
        (metastasis; EphA2 receptor Tyr kinase
        overexpression in prostatic neoplastic transformation)
IT
     Carcinoma
        (prostatic adenocarcinoma; EphA2 receptor Tyr
        kinase overexpression in prostatic neoplastic transformation)
IT
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (EphA2 receptor Tyr kinase overexpression
        in prostatic neoplastic transformation)
RE.CNT
              THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Andres, A; Oncogene 1994, V9, P1461 HCAPLUS
(2) Bostwick, D; Urologic Surgical Pathology 1997, P343
(3) Cantley, L; Cell 1991, V64, P281 HCAPLUS
(4) Carles-Kinch, K; Cancer Res 2002, V62, P2840 HCAPLUS
(5) Cheng, L; Am J Pathol 1996, V148, P1375 MEDLINE
(6) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
(7) Fleming, I; AJCC Cancer Staging Manual 1997, P219
(8) Gleason, D; J Urol 1974, V111, P58 MEDLINE
(9) Hunter, T; Cold Spring Harb Symp Quant Biol 1992, V57, P25 HCAPLUS
(10) Hunter, T; Curr Opin Cell Biol 1989, V6, P1168
(11) Jiang, J; Am J Pathol 2002, V160, P667 HCAPLUS
(12) Kinch, M; Clin Cancer Res 2003, V9, P613 HCAPLUS
(13) Kinch, M; Clin Cancer Res 2003, V9, P613 HCAPLUS
(14) Kinch, M; J Cell Biol 1995, V130, P461 HCAPLUS
(15) Kondapaka, B; Mol Cell Endocrinol 1996, V117, P53 HCAPLUS
(16) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
(17) Miyazaki, T; Int J Cancer 2003, V103, P657 HCAPLUS
(18) Nemoto, T; Pathobiology 1997, V65, P195 HCAPLUS
(19) Pasquale, E; Curr Opin Cell Biol 1997, V9, P608 HCAPLUS
(20) Robinson, D; Proc Natl Acad Sci USA 1996, V93, P5958 HCAPLUS
(21) Schlessinger, J; Neuron 1992, V9, P383 HCAPLUS
(22) Tremblay, L; Int J Cancer 1996, V68, P164 HCAPLUS
(23) Ullrich, A; Cell 1990, V61, P203 HCAPLUS
(24) Visakorpi, T; Mod Pathol 1992, V5, P643 MEDLINE
(25) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
(26) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
(27) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
(28) Zelinski, D; J Cell Biochem 2002, V85, P714 HCAPLUS
     ANSWER 14 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
L40
AN
     2003:982383 HCAPLUS
DN
     140:75821
ED
     Entered STN: 17 Dec 2003
TI
     EphA2 as Target of Anticancer Immunotherapy: Identification of
     HLA-A*0201-Restricted Epitopes
ΑU
     Alves, Pedro M. S.; Faure, Olivier; Graff-Dubois, Stephanie; Gross,
```

David-Alexandre; Cornet, Sebastien; Chouaib, Salem; Miconnet, Isabelle;

```
Lemonnier, Francois A.; Kosmatopoulos, Kostas
CS
     INSERM487, Institut Gustave Roussy, Villejuif, Fr.
     Cancer Research (2003), 63(23), 8476-8480
SO
     CODEN: CNREA8; ISSN: 0008-5472
PB
     American Association for Cancer Research
DT
     Journal
LA
     English
CC
     15-8 (Immunochemistry)
AB
     EphA2 (Eck) is a tyrosine kinase
     receptor that is overexpressed in several human cancers such as
     breast, colon, lung, prostate, gastric carcinoma, and metastatic melanoma
     but not in nonmalignant counterparts. To validate EphA2 as a
     tumor antigen recognized by CD8+ T lymphocytes, we used reverse immunol.
     approach to identify HLA-A*0201-restricted epitopes. Peptides bearing the
     HLA-A*0201-specific anchor motifs were analyzed for their capacity to bind
     and stabilize the HLA-A*0201 mols. Two peptides, EphA258 and EphA2550,
     with a high affinity for HLA-A*0201 were selected. Both peptides were
     immunogenic in the HLA-A*0201-transgenic HHD mice. Interestingly,
     peptide-specific murine CTLs cell lines responded to COS-7 cells
     coexpressing HLA-A*0201 and EphA2 and to EphA2-pos.
     human tumor cells of various origin (renal cell, lung, and colon carcinoma
     and sarcoma). This demonstrates that EphA258 and EphA2550 are naturally
     processed from endogenous EphA2. In addition, EphA258 and EphA2550
     stimulated specific CD8+ T cells from healthy donor peripheral blood
     mononuclear cells. These T cells recognized EphA2-pos. human
     tumor cells in an HLA-A*0201-restricted manner. Interestingly,
     EphA2-specific CD8+ T cells were detected in the peripheral blood
     mononuclear cells of prostate cancer patients. These results show for the
     first time that EphA2 is a tumor rejection antigen and lead us
     to propose EphA258 and EphA2550 peptides for a broad-spectrum-tumor
     immunotherapy.
ST
     EphA2 peptide anticancer immunotherapy
IT
     CD8-positive T cell
     Human
     MHC restriction
        (EphA2 as target of anticancer immunotherapy and
        identification of HLA-A*0201-restricted epitopes)
IT
     Immunotherapy
        (EphA2 as target of anticancer immunotherapy and
        identification of HLA-A*0201-restricted epitopes for)
IT
     Prostate gland, neoplasm
        (EphA2 as target of anticancer immunotherapy and
        identification of HLA-A*0201-restricted epitopes in)
IT
     Antigens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (tumor-rejection, EphA2; EphA2 as target of
        anticancer immunotherapy and identification of HLA-A*0201-restricted
        epitopes)
IT
     615266-60-9
                   615266-61-0
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (EphA2 as target of anticancer immunotherapy and
        identification of HLA-A*0201-restricted epitopes)
              THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
       31
RE
(1) Andersen, M; Cancer Res 2000, V61, P869
(2) Boon, T; Curr Opin Immunol 1997, V1997, P681
(3) Cheng, N; Mol Cancer Res 2002, V1, P2 HCAPLUS
(4) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS
(5) Dohn, M; Oncogene 2001, V20, P6503 HCAPLUS
(6) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
```

```
(7) Espevik, T; J Immunol Methods 1986, V95, P99 HCAPLUS
(8) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS
(9) Holder, N; Development (Camb) 1999, V126, P2033 HCAPLUS
(10) Hsu, F; Nat Med 1996, V2, P52 HCAPLUS
(11) Jager, E; Curr Opin Immunol 2002, V14, P178 HCAPLUS
(12) Kinch, M; Clin Cancer Res 2003, V9, P613 HCAPLUS
(13) Kugler, A; Nat Med 2000, V6, P332 HCAPLUS
(14) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
(15) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
(16) Miyazaki, T; Int J Cancer 2003, V103, P657 HCAPLUS
(17) Munoz, J; J Immunol 2002, V169, P177 HCAPLUS
(18) Nemoto, T; Pathobiology 1997, V65, P195 HCAPLUS
(19) Nestle, F; Nat Med 1998, V4, P328 HCAPLUS
(20) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
(21) Parham, P; Hum Immunol 1981, V3, P277 HCAPLUS
(22) Parker, K; J Immunol 1994, V152, P163 HCAPLUS
(23) Pascolo, S; J Exp Med 1997, V185, P2043 HCAPLUS
(24) Renkvist, N; Cancer Immunol Immunother 2001, V50, P3 HCAPLUS
(25) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
(26) Salgaller, M; Prostate 1998, V35, P144 MEDLINE
(27) Schmitz, M; Cancer Res 2000, V60, P4845 HCAPLUS
(28) Tourdot, S; Eur J Immunol 2000, V30, P3411 HCAPLUS
(29) Vonderheide, R; Immunity 1999, V10, P673 HCAPLUS
(30) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
(31) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
    ANSWER 15 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
L40
     2003:950865 HCAPLUS
AN
DN
     140:13032
ED
     Entered STN: 07 Dec 2003
     Low molecular weight protein tyrosine phosphatase
TI
     (LMW-PTP) as a diagnostic and therapeutic target
IN
     Kinch, Michael S.
PA
     Purdue Research Foundation, USA
SO
     PCT Int. Appl., 81 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM A61K038-00
     ICS A61K039-00; A61K039-395; G01N033-53
CC
     1-6 (Pharmacology)
     Section cross-reference(s): 9, 14
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                   DATE
     -----
                         ----
                                _____
                                            -----
                                          WO 2003-US16269
ΡI
     WO 2003099313
                         A1
                                20031204
                                                                   20030522 <--
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2486615
                                20031204
                                           CA 2003-2486615
                          AA
                                                                   20030522 <--
    EP 1505999
                         Α1
                                20050216
                                           EP 2003-734142
                                                                   20030522 <--
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
```

```
PRAI US 2002-382988P
                         P
                               20020523 <--
    WO 2003-US16269
                         W
                               20030522
CLASS
               CLASS PATENT FAMILY CLASSIFICATION CODES
PATENT NO.
 _____
                ____
WO 2003099313 ICM
                       A61K038-00
                       A61K039-00; A61K039-395; G01N033-53
                ICS
WO 2003099313 ECLA
                       A61K038/17A2; C12N009/16; G01N033/50D4; G01N033/574 <--
    Low mol. weight protein tyrosine phosphatase (LMW-PTP) is
     identified as a novel diagnostic and therapeutic target in cancer
     diagnosis, prognosis and treatment. The invention provides diagnostic and
     treatment methods useful in connection with cancers expressing LMW-PTP
     and, optionally, EphA2 receptor. Also provided is a
     screening method that utilizes changes in the amount and/or activity of
    LMW-PTP to identify candidate cancer therapeutic agents that effectively
     target the oncoprotein EphA2.
ST
    protein tyrosine phosphatase cancer diagnosis
    therapeutic target
IT
    Tyrosine kinase receptors
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor
        2; low mol. weight protein tyrosine
       phosphatase (LMW-PTP) as a diagnostic and therapeutic target for cancer
       and inhibition of EphA2 receptor in relation to
       conjugation with cytotoxic agents)
    Adhesion, biological
TΤ
        (focal, LMW-PTP overexpression increase of; low mol. weight
       protein tyrosine phosphatase (LMW-PTP) as a
       diagnostic and therapeutic target for cancer and inhibition of
       EphA2 receptor in relation to conjugation with
       cytotoxic agents)
IT
    Antitumor agents
    Cytotoxic agents
    Diagnosis
    Drug interactions
    Human
    Neoplasm
        (low mol. weight protein tyrosine phosphatase
        (LMW-PTP) as a diagnostic and therapeutic target for cancer and
        inhibition of EphA2 receptor in relation to
       conjugation with cytotoxic agents)
IT
    Carcinoma
        (metastasis; low mol. weight protein tyrosine
       phosphatase (LMW-PTP) as a diagnostic and therapeutic target for cancer
       and inhibition of EphA2 receptor in relation to
       conjugation with cytotoxic agents)
IT
    Phosphorylation, biological
        (of EphA2 receptor tyrosines; low mol.
       weight protein tyrosine phosphatase (LMW-PTP) as a
       diagnostic and therapeutic target for cancer and inhibition of
       EphA2 receptor in relation to conjugation with
       cytotoxic agents)
IT
    Organelle
        (stress fiber, LMW-PTP overexpression increase of; low mol. weight
       protein tyrosine phosphatase (LMW-PTP) as a
       diagnostic and therapeutic target for cancer and inhibition of
       EphA2 receptor in relation to conjugation with
       cytotoxic agents)
IT
    149433-91-0, EphA2 receptor tyrosine
    kinase
```

```
RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (low mol. weight protein tyrosine phosphatase
        (LMW-PTP) as a diagnostic and therapeutic target for cancer and
        inhibition of EphA2 receptor in relation to
        conjugation with cytotoxic agents)
IT
     352548-19-7, Low molecular weight protein tyrosine
     phosphatase
     RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL
     (Biological study); USES (Uses)
        (low mol. weight protein tyrosine phosphatase
        (LMW-PTP) as a diagnostic and therapeutic target for cancer and
        inhibition of EphA2 receptor in relation to
        conjugation with cytotoxic agents)
IT
     630435-42-6
                   630435-43-7
                                 630435-44-8
     RL: PRP (Properties)
        (unclaimed nucleotide sequence; low mol. weight protein
        tyrosine phosphatase (LMW-PTP) as a diagnostic and therapeutic
        target)
RE.CNT
              THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Andersen; US 5958957 A 1999 HCAPLUS
(2) Caselli; J Biol Chem 1998, V273(49), P32554 HCAPLUS
(3) Chiarugi; J Biol Chem March 1998, V273(12), P6776 HCAPLUS
(4) Fiaschi; J Biol Chem 2001, V276(52), P49156 HCAPLUS
(5) Stein; Genes and Develop 1998, V12(5), P667 HCAPLUS
L40 ANSWER 16 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2003:933787 HCAPLUS
DN
     140:268478
     Entered STN: 01 Dec 2003
ED
     EphA2 Up-regulation induced by deoxycholic acid in human colon
ΤI
     carcinoma cells, an involvement of extracellular signal-regulated
     kinase and p53-independence
ΑU
     Li, Zhongyou; Tanaka, Masamitsu; Kataoka, Hideki; Nakamura, Ritsuko;
     Sanjar, Ravshanov; Shinmura, Kazuya; Sugimura, Haruhiko
CS
     The First Department of Pathology, Hamamatsu University School of
     Medicine, Hamamatsu, 431-3192, Japan
     Journal of Cancer Research and Clinical Oncology (2003),
SO
     129(12), 703-708
     CODEN: JCROD7; ISSN: 0171-5216
PB
     Springer-Verlag
     Journal
DT
LΑ
     English
CC
     14-1 (Mammalian Pathological Biochemistry)
AB
     Purpose: The EphA2 receptor protein
     tyrosine kinase gene has been shown to be over-expressed
     or functionally altered in a number of human tumors, including colon cancer,
     but little is known about the regulation of this new oncoprotein.
     order to explore the mechanism of EphA2 up-regulation in cancer
     cells, we examined the change of expression of EphA2 gene induced
     by deoxycholic acid (DCA) and elucidated its possible pathways in human
     colon cancer cells. Methods: Western blot and RT-PCR were used to assess
     the protein expression and mRNA in several colon cancer cell
     lines, which harbor various p53 status. The inhibition study to
     interfere the MAPK pathway was performed by using various chems. and by
     transfecting dominant neg. mutant plasmids. Results: Up-regulation of
     EphA2 induced by DCA was observed in a dose- and time-dependent
```

constant regardless of p53 status including wild, mutant or knocked out in

fashion both in mRNA and protein levels. This regulation is

the colon cell lines used. This induction was in part blocked

ST

IT

IT

IT

IT

IT

IT

IT

IT

RE

by either erk1/2 inhibitors or dominant neg. mutants erk1/2 plasmids. Conclusions: These results suggest that DCA induced up-regulation of EphA2 in colon cancer cells is due to activation of erk1/2 cascade, and is p53-independent. Taken together with the roles of EphA2 and DCA in tumorigenesis, which have been independently reported, our observation will provide a new mechanistic basis of DCA commitment in carcinogenesis. EphA2 deoxycholate ERK kinase colon carcinoma Signal transduction, biological Transformation, neoplastic (EphA2 up-regulation induced by deoxycholic acid in human colon carcinoma cells, an involvement of extracellular signal-regulated kinase and p53-independence) p53 (protein) RL: BSU (Biological study, unclassified); BIOL (Biological study) (EphA2 up-regulation induced by deoxycholic acid in human colon carcinoma cells, an involvement of extracellular signal-regulated **kinase** and p53-independence) Transcriptional regulation (activation; EphA2 up-regulation induced by deoxycholic acid in human colon carcinoma cells, an involvement of extracellular signal-regulated kinase and p53-independence) Intestine, neoplasm (colon, carcinoma; EphA2 up-regulation induced by deoxycholic acid in human colon carcinoma cells, an involvement of extracellular signal-regulated kinase and p53-independence) Carcinoma (colon; EphA2 up-regulation induced by deoxycholic acid in human colon carcinoma cells, an involvement of extracellular signal-regulated kinase and p53-independence) Tyrosine kinase receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (ephrin type-A receptor 2; EphA2 up-regulation induced by deoxycholic acid in human colon carcinoma cells, an involvement of extracellular signal-regulated kinase and p53-independence) 83-44-3, Deoxycholic acid RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study) (EphA2 up-regulation induced by deoxycholic acid in human colon carcinoma cells, an involvement of extracellular signal-regulated kinase and p53-independence) 137632-07-6, Erk1 kinase 137632-08-7, Erk2 kinase RL: BSU (Biological study, unclassified); BIOL (Biological study) (EphA2 up-regulation induced by deoxycholic acid in human colon carcinoma cells, an involvement of extracellular signal-regulated kinase and p53-independence) RE.CNT THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Adachi, M; Embo J 1999, V18, P5347 HCAPLUS (2) Bunz, F; Science 1998, V282, P1497 HCAPLUS (3) Cheng, N; Cytokine Growth Factor Rev 2002, V13, P75 HCAPLUS (4) Crowley-Weber, C; Carcinogenesis 2002, V23, P2063 HCAPLUS (5) Debruyne, P; Mutat Res 2001, V480/481, P359 (6) Dobashi, Y; Mol Pathol 1994, V3, P9 MEDLINE (7) Dohn, M; Oncogene 2001, V20, P6503 HCAPLUS (8) Holder, N; Development 1999, V126, P2033 HCAPLUS

(9) Lechner, S; Carcinogenesis 2002, V23, P1281 HCAPLUS

(10) Li, Z; Cancer Lett 2002, V177, P203 HCAPLUS

- (11) Liu, W; Cancer 2002, V94, P934 HCAPLUS
- (12) Martinez, J; Nutr Cancer 1998, V31, P111 HCAPLUS
- (13) Qiao, D; Carcinogenesis 2001, V22, P35 HCAPLUS
- (14) Qiao, L; Mol Biol Cell 2001, V12, P2629 HCAPLUS
- (15) Robbins, D; J Biol Chem 1993, V268, P5097 HCAPLUS
- (16) Robinson, M; Biochemistry 1996, V35, P5641 HCAPLUS
- (17) Stephenson, S; BMC Mol Biol 2001, V2, P15 MEDLINE
- (18) Walker-Daniels, J; Am J Pathol 2003, V162, P1037 HCAPLUS
- (19) Walker-Daniels, J; Mol Cancer Res 2002, V1, P79 HCAPLUS
- (20) Wang, Y; Biochem Biophys Res Commun 2002, V296, P214 HCAPLUS
- (21) Yoon, J; Gastroenterology 2002, V122, P985 HCAPLUS
- (22) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
- (23) Zelinski, D; J Cell Biochem 2002, V85, P714 HCAPLUS
- L40 ANSWER 17 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2003:917659 HCAPLUS
- DN 140:57464
- ED Entered STN: 24 Nov 2003
- TI Differential **EphA2** Epitope Display on Normal versus Malignant Cells
- AU Coffman, Karen T.; Hu, Min; Carles-Kinch, Kelly; Tice, David; Donacki, Nanci; Munyon, Karyn; Kifle, Giza; Woods, Robert; Langermann, Solomon; Kiener, Peter A.; Kinch, Michael S.
- CS MedImmune, Inc., Gaithersburg, MD, USA
- SO Cancer Research (2003), 63(22), 7907-7912 CODEN: CNREA8; ISSN: 0008-5472
- PB American Association for Cancer Research
- DT Journal
- LA English

AΒ

- CC 14-1 (Mammalian Pathological Biochemistry)
 Section cross-reference(s): 15
 - The EphA2 receptor tyrosine kinase is overexpressed in many different types of human cancers where it functions as a powerful oncoprotein. Dramatic changes in the subcellular localization and function of EphA2 have also been linked with cancer, and in particular, unstable cancer cell-cell contacts prevent EphA2 from stably binding its ligand on the surface of adjoining cells. This change is important in light of evidence that ligand binding causes EphA2 to transmit signals that neq. regulate tumor cell growth and invasiveness and also induce EphA2 degradation On the basis of these properties, the authors have begun to target EphA2 on tumor cells using agonistic antibodies, which mimic the consequences of ligand binding. In our present study, the authors show that a subset of agonistic EphA2 antibodies selectively bind epitopes on malignant cells, which are not available on nontransformed epithelial The authors also show that such epitopes arise from differential cell-cell adhesions and that the stable intercellular junctions of nontransformed epithelial cells occlude the binding site for ligand, as well as this subset of EphA2 antibodies. Finally, the authors demonstrate that antibody targeting of EphA2 decreases tumor cell growth as measured using xenograft tumor models and found that the mechanism of antibody action relates to EphA2 protein degradation in vivo. Taken together, these results suggest new opportunities for therapeutic targeting of the large number of different cancers that express EphA2 in a manner that could minimize potential toxicities to normal cells.
- ST EphA2 receptor epitope cancer
- IT Antitumor agents Epitopes

Human

```
Neoplasm
        (differential EphA2 epitope display on normal vs. malignant
        cells)
     Adhesion, biological
IT
        (differential EphA2 epitope display on normal vs. malignant
        cells in relation to)
IT
     Cell junction
        (differential EphA2 epitope display on normal vs. malignant
        cells in relation to stable intercellular junctions of normal cells)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor
        2; differential EphA2 epitope display on normal vs.
        malignant cells)
RE.CNT
              THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Carles-Kinch, K; Cancer Res 2002, V62, P2840 HCAPLUS
(2) Davis, S; Science (Wash DC) 1994, V266, P816 HCAPLUS
(3) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
(4) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS
(5) Kinch, M; Cell Adhes Commun 1997, V4, P425 HCAPLUS
(6) Kinch, M; Clin Cancer Res 2003, V9, P613 HCAPLUS
(7) Kinch, M; Clin Exp Metastasis 2003, V20, P59 HCAPLUS
(8) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
(9) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
(10) Miyazaki, T; Int J Cancer 2003, V103, P657 HCAPLUS
(11) Nakamoto, M; Microsc Res Tech 2002, V59, P58 HCAPLUS
(12) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
(13) Walker-Daniels, J; Am J Pathol 2003, V162, P1037 HCAPLUS
(14) Walker-Daniels, J; Mol Cancer Res 2002, V1, P79 HCAPLUS
(15) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
(16) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
(17) Zantek, N; Clin Cancer Res 2001, V7, P3640 HCAPLUS
(18) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
(19) Zetter, B; Semin Cancer Biol 1993, V4, P219 HCAPLUS
(20) Zschiesche, W; Anticancer Res 1997, V17, P561 MEDLINE
    ANSWER 18 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
ΑN
     2003:912959 HCAPLUS
DN
     139:394888
ED
     Entered STN: 21 Nov 2003
ΤI
     Anti-EphA2 protein monoclonal antibodies for
     diagnosis, prognosis and therapy of cancer and metastasis
IN
     Kinch, Michael S.; Carles-Kinch, Kelly; Kiener, Peter;
     Langermann, Solomon
PA
    Medimmune, Inc., USA
     PCT Int. Appl., 175 pp.
so
     CODEN: PIXXD2
DT
     Patent
LA
     English
TC
     ICM A61K
CC
     15-3 (Immunochemistry)
     Section cross-reference(s): 1, 8, 9
FAN.CNT 1
     PATENT NO.
                        KIND
                               DATE
                                           APPLICATION NO.
                                                                   DATE
     ------
                                            -----
                                                                   -----
PΙ
    WO 2003094859
                         A2
                                20031120
                                            WO 2003-US15044
                                                                   20030512 <--
     WO 2003094859
                        A3
                                20050203
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
```

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

```
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                               20031120
                                          CA 2003-2485373
     CA 2485373
                         AΑ
                                                                 20030512 <--
                                          US 2003-436782
    US 2004028685
                         A1
                                20040212
                                                                  20030512 <--
                                          EP 2003-750125
     EP 1519956
                         A2
                               20050406
                                                                  20030512 <--
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI US 2002-379322P
                        P
                               20020510 <--
    US 2002-418213P
                         P
                               20021014 <--
    US 2003-460507P
                         P
                               20030403 <--
    WO 2003-US15044
                         W
                               20030512
CLASS
PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
                _____
WO 2003094859
                ICM
                       A61K
WO 2003094859
                ECLA
                       C07K016/28H
                                                                           <--
US 2004028685
                NCL
                       424/155.100
                ECLA
                       C07K016/28H
AΒ
     The present invention relates to methods and compns. designed for the
     treatment, management, or prevention of cancer, particularly, metastatic
     cancer. In one embodiment, the methods of the invention comprise the
     administration of an effective amount of an antibody that binds to
     EphA2 and agonizes EphA2, thereby increasing
     EphA2 phosphorylation and decreasing EphA2 levels.
     other embodiments, the methods of the invention comprise the
     administration of an effective amount of an antibody that binds to
     EphA2 and inhibits cancer cell colony formation in soft agar,
     inhibits tubular network formation in three-dimensional basement membrane
     or extracellular matrix preparation, preferentially binds to an EphA2
     epitope that is exposed on cancer cells but not non-cancer cells, and/or
     has a low Koff, thereby, inhibiting tumor cell growth and/or metastasis.
     The invention also provides pharmaceutical compns. comprising one or more
     EphA2 antibodies of the invention either alone or in combination
     with one or more other agents useful for cancer therapy.
ST
     EphA2 protein epitope monoclonal antibody cancer
     metastasis therapy
IT
     Inflammation
        (Crohn's disease; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
     Intestine, disease
        (Crohn's; anti-EphA2 protein monoclonal antibodies
        for diagnosis, prognosis and therapy of cancer and metastasis)
IT
     Hybridoma
        (Eph099B-102.147; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
    Hybridoma
IT
        (Eph099B-208.261; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
     Hybridoma
IT
        (Eph099B-210.248; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
```

```
metastasis)
ΤT
     Hybridoma
        (Eph099B-233.152; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
     Animal cell
     Animal cell line
     Animal tissue
     Antitumor agents
     Apoptosis
     Asthma
     Bladder, neoplasm
     Blood cell
     Blood serum
     Carcinoma
     Carcinoma
     Chemotherapy
     Epitopes
     Extracellular matrix
     Genetic vectors
     Human
     Imaging
     Immunotherapy
     Lung, neoplasm
     Mammary gland, neoplasm
     Melanoma
     Molecular cloning
     Necrosis
     Pancreas, neoplasm
     Phosphorylation, biological
     Prognosis
     Prostate gland, neoplasm
       Protein sequences
     Psoriasis
     Radiotherapy
     Skin, neoplasm
     Sputum
     Surgery
     Urine
     cDNA sequences
        (anti-EphA2 protein monoclonal antibodies for
        diagnosis, prognosis and therapy of cancer and metastasis)
IT
     Antibodies and Immunoglobulins
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (anti-EphA2 protein monoclonal antibodies for
        diagnosis, prognosis and therapy of cancer and metastasis)
IT
     Fibronectins
     Ligands
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (anti-EphA2 protein monoclonal antibodies for
        diagnosis, prognosis and therapy of cancer and metastasis)
     Antisense oligonucleotides
IT
     Nucleic acids
     RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (anti-EphA2 protein monoclonal antibodies for
        diagnosis, prognosis and therapy of cancer and metastasis)
IT
     Basement membrane
```

```
(artificial; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
    Needles (tools)
        (aspirates; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
    Health products
IT
        (biologicals; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
    Diagnosis
        (cancer; anti-EphA2 protein monoclonal antibodies
        for diagnosis, prognosis and therapy of cancer and metastasis)
IT
    Drug delivery systems
        (carriers; anti-EphA2 protein monoclonal antibodies
        for diagnosis, prognosis and therapy of cancer and metastasis)
IT
    Biology
        (cell, host; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
    Lung, disease
TТ
        (chronic obstructive; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
    Intestine, neoplasm
        (colon; anti-EphA2 protein monoclonal antibodies
        for diagnosis, prognosis and therapy of cancer and metastasis)
IT
     Physical properties
        (consts., Koff; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
    Tyrosine kinase receptors
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic
    use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
        (ephrin type-A receptor
        2; anti-EphA2 protein monoclonal antibodies
        for diagnosis, prognosis and therapy of cancer and metastasis)
IT
     Cytometry
        (flow; anti-EphA2 protein monoclonal antibodies for
        diagnosis, prognosis and therapy of cancer and metastasis)
IT
    Antibodies and Immunoglobulins
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (fragments; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
    Antibodies and Immunoglobulins
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (fusion products; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
    Antibodies and Immunoglobulins
    RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (heavy chain; anti-EphA2 protein monoclonal
```

```
antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
     Antibodies and Immunoglobulins
IT
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (humanized; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
TT
    Diagnosis
        (immunodiagnosis; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
     Immunoassay
        (immunofluorescence microscopy; anti-EphA2 protein
        monoclonal antibodies for diagnosis, prognosis and therapy of cancer
        and metastasis)
IT
     Intestine, disease
        (inflammatory; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
     Antibodies and Immunoglobulins
     RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (light chain; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
    Neoplasm
        (metastasis; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
ΙT
     Antibodies and Immunoglobulins
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (monoclonal; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
    Disease, animal
        (proliferative, hyper-; anti-EphA2 protein
        monoclonal antibodies for diagnosis, prognosis and therapy of cancer
        and metastasis)
IT
     Kidney, neoplasm
        (renal cell carcinoma; anti-EphA2 protein
        monoclonal antibodies for diagnosis, prognosis and therapy of cancer
        and metastasis)
TΤ
     Carcinoma
        (renal cell; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
    Artery, disease
        (restenosis, smooth muscle; anti-EphA2 protein
        monoclonal antibodies for diagnosis, prognosis and therapy of cancer
        and metastasis)
IT
    Muscle, disease
        (smooth, restenosis; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
    Hormones, animal, biological studies
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
```

```
(Biological study); USES (Uses)
        (therapy; anti-EphA2 protein monoclonal antibodies
        for diagnosis, prognosis and therapy of cancer and metastasis)
IT
     Imaging
        (tumor; anti-EphA2 protein monoclonal antibodies
        for diagnosis, prognosis and therapy of cancer and metastasis)
ΙT
     625867-94-9P
                    625867-95-0P
                                   625867-98-3P
                                                  625867-99-4P
     625868-03-3P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (amino acid sequence; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
TΤ
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: ARU (Analytical role, unclassified); BSU (Biological study,
     unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic
     use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
        (anti-EphA2 protein monoclonal antibodies for
        diagnosis, prognosis and therapy of cancer and metastasis)
TT
     119978-18-6, Matrigel
     RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST
     (Analytical study); USES (Uses)
        (anti-EphA2 protein monoclonal antibodies for
        diagnosis, prognosis and therapy of cancer and metastasis)
TΤ
     157597-32-5
                   176714-45-7
                                 384331-85-5
                                              500757-49-3
                                                            625812-75-1
     625812-76-2
                   625812-77-3
                                 625812-78-4
                                               625812-79-5
                                                             625812-80-8
     625812-81-9
                   625812-82-0
                                 625812-83-1
                                               625812-84-2
                                                             625812-85-3
     625812-86-4
                   625812-87-5
                                 625812-88-6
                                               625862-83-1
     RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (anti-EphA2 protein monoclonal antibodies for
        diagnosis, prognosis and therapy of cancer and metastasis)
TΤ
     625867-96-1P
                    625867-97-2P
                                   625868-00-0P
                                                  625868-01-1P 625868-04-4P
     625868-05-5P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (nucleotide sequence; anti-EphA2 protein monoclonal
        antibodies for diagnosis, prognosis and therapy of cancer and
        metastasis)
IT
     9002-18-0, Agar
     RL: ARU (Analytical role, unclassified); DEV (Device component use); DGN
     (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES
     (Uses)
        (soft; anti-EphA2 protein monoclonal antibodies for
        diagnosis, prognosis and therapy of cancer and metastasis)
IT
     625868-09-9
                   625868-10-2
                                 625868-11-3
                                                             625868-13-5
                                               625868-12-4
                   625868-15-7
     625868-14-6
                                 625868-16-8
                                               625868-17-9
                                                             625868-18-0
     625868-19-1
                   625868-20-4
                                 625868-21-5
                                               625868-22-6
                                                             625868-23-7
                   625868-25-9
                                 625868-26-0
                                               625868-27-1
     625868-24-8
     RL: PRP (Properties)
        (unclaimed nucleotide sequence; anti-EphA2 protein
        monoclonal antibodies for diagnosis, prognosis and therapy of cancer
        and metastasis)
L40 ANSWER 19 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2003:837593 HCAPLUS
DN
     139:322275
```

```
ED
    Entered STN: 26 Oct 2003
TI
    Peptide T epitopes of the EphA2 antigen for antitumor
    immunotherapy
IN
    Kosmatopoulos, Kostas; Alves, Pedro
    Institut National de la Sante et de la Recherche Medicale INSERM, Fr.;
PA
    Institut Gustave Roussy
SO
    Fr. Demande, 22 pp.
    CODEN: FRXXBL
DT
    Patent
    French
LΑ
IC
    ICM C07K007-06
    ICS C12N015-12; A61K039-00; A61K048-00; A61K031-7105; A61K031-711;
         A61P035-00; A61P037-04
CC
    15-2 (Immunochemistry)
    Section cross-reference(s): 1
FAN.CNT 1
                                        APPLICATION NO.
    PATENT NO.
                      KIND DATE
                                                              DATE
                      ---- ------
                                        -----
PΙ
    FR 2838742
                       A1 20031024 FR 2002-5048
                                                               20020423 <--
                       B1 20040709
    FR 2838742
                                         CA 2003-2482930
                       AA
    CA 2482930
                              20031106
                                                              20030423 <--
                       A2 20031106
A3 20040401
    WO 2003091383
                              20031106 WO 2003-FR1280
                                                              20030423 <--
    WO 2003091383
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
            PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
            TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    EP 1497417
                       A2 20050119 EP 2003-740654 20030423 <--
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI FR 2002-5048
                    Α
                            20020423
                                       <--
    WO 2003-FR1280
                        W.
                              20030423
CLASS
PATENT NO.
             CLASS PATENT FAMILY CLASSIFICATION CODES
 _____
                      -----
FR 2838742
                      C07K007-06
              ICM
                ICS
                      C12N015-12; A61K039-00; A61K048-00; A61K031-7105;
                      A61K031-711; A61P035-00; A61P037-04
                      C07K014/715
FR 2838742
              ECLA
                                                                        <--
WO 2003091383 ECLA
                      C07K014/715
                                                                        <--
AB
    The invention discloses peptides constituting EphA2 antigen T
    epitopes, presented by MHC I. The peptides are useful in particular for
    antitumor immunotherapy.
ST
    antitumor immunotherapy peptide T epitope EphA2 antigen
IT
    Lung, neoplasm
       (1355 cell; peptide T epitopes of EphA2 antigen for antitumor
       immunotherapy)
IT
    Histocompatibility antigens
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
       (HLA-A, HLA-A*0201; peptide T epitopes of EphA2 antigen for
       antitumor immunotherapy)
    Prostate gland, neoplasm
IT
       (LNCaP and DU145 cells; peptide T epitopes of EphA2 antigen
       for antitumor immunotherapy)
```

```
IT
     Histocompatibility antigens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (MHC (major histocompatibility complex), class I; peptide T epitopes of
        EphA2 antigen for antitumor immunotherapy)
IT
     Sarcoma
        (SAOS cell; peptide T epitopes of EphA2 antiqen for antitumor
        immunotherapy)
IT
     Intestine, neoplasm
        (colon, Caco-2 cell; peptide T epitopes of EphA2 antigen for
        antitumor immunotherapy)
IT
     T cell (lymphocyte)
        (cytotoxic; peptide T epitopes of EphA2 antigen for antitumor
        immunotherapy)
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin type-A receptor
        2; peptide T epitopes of EphA2 antigen for antitumor
        immunotherapy)
IT
     Drug delivery systems
     Epitopes
     Human
     Immunotherapy
        (peptide T epitopes of EphA2 antigen for antitumor
        immunotherapy)
IT
     Fusion proteins (chimeric proteins)
     Peptides, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (peptide T epitopes of EphA2 antigen for antitumor
        immunotherapy)
IT
     Polynucleotides
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (peptide-encoding; peptide T epitopes of EphA2 antigen for
        antitumor immunotherapy)
IT
     Kidney, neoplasm
        (renal cell carcinoma; peptide T epitopes of EphA2 antigen
        for antitumor immunotherapy)
IT
        (renal cell; peptide T epitopes of EphA2 antigen for
        antitumor immunotherapy)
IT
     Vaccines
        (tumor; peptide T epitopes of EphA2 antigen for antitumor
        immunotherapy)
IT
     Antitumor agents
        (vaccines; peptide T epitopes of EphA2 antiqen for antitumor
        immunotherapy)
TT
     615266-60-9
                   615266-61-0
     RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (peptide T epitopes of EphA2 antigen for antitumor
        immunotherapy)
RE.CNT
              THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Hiroaki, H; JOURNAL OF BIOMOLECULAR NMR 1996, V8(2), P105 HCAPLUS
(2) Lindberg, R; MOLECULAR AND CELLULAR BIOLOGY 1990, V10(12), P6316 HCAPLUS
(3) Ye, J; US 6323016 B1 2001 HCAPLUS
(4) Ye, J; US 2002025570 A1 2002 HCAPLUS
L40 ANSWER 20 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2003:613807 HCAPLUS
DN
     139:275676
```

```
ED Entered STN: 11 Aug 2003
```

- TI Disease Stage Variation in CD4+ and CD8+ T-Cell Reactivity to the Receptor Tyrosine Kinase EphA2 in Patients with Renal Cell Carcinoma
- AU Tatsumi, Tomohide; Herrem, Christopher J.; Olson, Walter C.; Finke, James H.; Bukowski, Ronald M.; Kinch, Michael S.; Ranieri, Elena; Storkus, Walter J.
- CS Departments of Surgery and Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, 15213, USA
- SO Cancer Research (2003), 63(15), 4481-4489 CODEN: CNREA8; ISSN: 0008-5472
- PB American Association for Cancer Research
- DT Journal
- LA English
- CC 15-10 (Immunochemistry)
 Section cross-reference(s): 14
- The authors have evaluated CD8+ and CD4+ T-cell responses against a new AB tumor-associated antigen, the receptor tyrosine kinase EphA2, which is broadly expressed in diverse cancer histologies and is frequently overexpressed in advanced stage/metastatic disease. They report herein that EphA2 is overexpressed in renal cell carcinoma (RCC) cell lines and clin. specimens of RCC, and find that the highest levels of EphA2 are consistently found in the most advanced stages of the disease. The authors identified and synthesized 5 putative HLA class I-binding and 3 class II-binding peptides derived from EphA2 that might serve as targets for immune reactivity. Each peptide induced specific, tumor-reactive CD8+ or CD4+T-cell responses as measured using IFN- γ enzyme-linked immunospot assays. The EphA2 peptides elicited relatively weak responses from CD8+ T cells derived from normal healthy volunteers or from RCC patients with active disease. In marked contrast, immune reactivity to EphA2-derived epitopes was greatly enhanced in CD8+ T cells that had been isolated from patients who were rendered disease-free, after surgery. Furthermore, enzyme-linked immunospot analyses demonstrated prominent EphA2-restricted T-helper 1-type CD4+ T cell activity in patients with early stage disease, whereas T-helper 2-type and T regulatory-type responses predominated in patients with more advanced forms of RCC. Thus, the immune system of cancer patients actively monitors EphA2-derived epitopes, and the magnitude and character of T-cell responses to EphA2 epitopes may convey much-needed predictive information about disease stage and
- ST T cell receptor tyrosine kinase EphA2 kidney carcinoma prognosis
- IT CD4-positive T cell CD8-positive T cell

Epitopes

outcome.

Human

(disease stage variation in CD4+ and CD8+ T-cell reactivity to tumor antigen receptor tyrosine kinase

EphA2 in patients with renal cell carcinoma)

IT Tumor antigens

Tumor antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study) (disease stage variation in CD4+ and CD8+ T-cell reactivity to tumor antigen receptor tyrosine kinase

EphA2 in patients with renal cell carcinoma)

IT Prognosis

(disease stage variation in CD4+ and CD8+ T-cell reactivity to tumor antigen receptor tyrosine kinase

```
EphA2 in patients with renal cell carcinoma in relation to)
IT
     Kidney, neoplasm
        (renal cell carcinoma; disease stage variation in CD4+ and CD8+ T-cell
        reactivity to tumor antigen receptor tyrosine
        kinase EphA2 in patients with renal cell carcinoma)
TT
     Carcinoma
        (renal cell; disease stage variation in CD4+ and CD8+ T-cell reactivity
        to tumor antigen receptor tyrosine kinase
        EphA2 in patients with renal cell carcinoma)
IT
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (disease stage variation in CD4+ and CD8+ T-cell reactivity to tumor
        antigen receptor tyrosine kinase
        EphA2 in patients with renal cell carcinoma)
TΤ
     604797-13-9
                   604797-14-0
                                 604797-15-1
                                               604797-16-2
                                                              604797-17-3
     604797-18-4
                   604797-19-5
                                 604797-20-8
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (disease stage variation in CD4+ and CD8+ T-cell reactivity to tumor
        antigen receptor tyrosine kinase
        EphA2 in patients with renal cell carcinoma)
RE.CNT
        56
              THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bittner, M; Nature (Lond) 2000, V406, P536 HCAPLUS
(2) Boel, P; Immunity 1995, V2, P167 HCAPLUS
(3) Boon, T; Curr Opin Immunol 1997, V9, P681 HCAPLUS
(4) Boon, T; J Exp Med 1996, V183, P725 HCAPLUS
(5) Brichard, V; J Exp Med 1993, V178, P489 HCAPLUS
(6) Chaux, P; J Exp Med 1999, V189, P767 HCAPLUS
(7) Cheever, M; Immunol Rev 1995, V145, P33 HCAPLUS
(8) Chen, Y; Proc Natl Acad Sci USA 1997, V94, P1914 HCAPLUS
(9) Coulie, P; Proc Natl Acad Sci USA 2001, V98, P10290 HCAPLUS
(10) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS
(11) D'Amico, T; Ann Thorac Surg 2001, V72, P1144 MEDLINE
(12) Easty, D; Cancer Res 1995, V55, P2528 HCAPLUS
(13) Easty, D; Int J Cancer 1999, V84, P494 HCAPLUS
(14) Elsasser-Beile, U; Tumor Biol 1998, V19, P470 HCAPLUS
(15) Eph Nomenclature Committee; Cell 1997, V90, P403
(16) Finke, J; J Immunother Emphas Tumor Immunol 1994, V15, P91 HCAPLUS
(17) Gnjatic, S; J Immunol 1998, V160, P328 HCAPLUS
(18) Honeyman, M; Nat Biotechnol 1998, V16, P966 HCAPLUS
(19) Jager, E; J Exp Med 2000, V191, P625 HCAPLUS
(20) Jager, E; Proc Natl Acad Sci USA 2000, V97, P12198 HCAPLUS
(21) Kawakami, Y; J Immunol 1995, V154, P3961 HCAPLUS
(22) Kawakami, Y; Proc Natl Acad Sci USA 1994, V91, P3515 HCAPLUS
(23) Keilholz, U; J Immunother 2002, V25, P97
(24) Kiessling, R; Cancer Immunol Immunother 1999, V48, P353 HCAPLUS
(25) Knoll, B; Development 2000, V128, P895
(26) Kolbeck, P; Mod Pathol 1992, V5, P420 MEDLINE
(27) Krause, I; Crit Rev Immunol 2000, V20, P1 HCAPLUS
(28) Levings, M; J Exp Med 2002, V196, P1335 HCAPLUS
(29) Liu, H; J Immunol 2002, V168, P3477 HCAPLUS
(30) Maeurer, M; Cancer Immunol Immunother 1995, V41, P111 HCAPLUS
(31) Mellitzer, G; Curr Opin Neurobiol 2000, V10, P400 HCAPLUS
(32) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
(33) Miyazaki, T; Int J Cancer 2003, V103, P657 HCAPLUS
(34) Moser, J; Viral Immunol 2001, V14, P199 HCAPLUS
(35) Nestle, F; Nat Med 1998, V4, P328 HCAPLUS
(36) Oba, S; Cancer Lett 2001, V164, P97 HCAPLUS
```

- (37) Ogawa, K; Oncogene 2003, V19, P6043
- (38) Pardoll, D; Curr Opin Immunol 1998, V10, P588 HCAPLUS
- (39) Pieper, R; J Exp Med 1999, V189, P757 HCAPLUS
- (40) Ryan, M; Kidney Int 1994, V45, P48 MEDLINE
- (41) Southwood, S; J Immunol 1998, V160, P3363 HCAPLUS
- (42) Tatsumi, T; J Exp Med 2002, V196, P619 HCAPLUS
- (43) Toes, R; J Exp Med 1999, V189, P753 HCAPLUS
- (44) Topalian, S; J Exp Med 1996, V183, P1965 HCAPLUS
- (45) Topalian, S; Proc Natl Acad Sci USA 1994, V91, P9461 HCAPLUS
- (46) Van den Eynde, B; J Exp Med 1995, V182, P689 HCAPLUS
- (47) Van den Hove, L; Clin Exp Immunol 1997, V109, P501 MEDLINE
- (48) Vieira, P; J Immunol 2000, V164, P4507 HCAPLUS
- (49) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
- (50) Wang, R; Science (Wash DC) 1999, V284, P1351 HCAPLUS
- (51) Willkinson, D; Nat Rev Neurosci 2001, V2, P155
- (52) Wolfel, T; Science (Wash DC) 1995, V269, P1281 MEDLINE
- (53) Yu, J; Cancer Res 2001, V61, P842 HCAPLUS
- (54) Zantek, N; Clin Cancer Res 2001, V7, P3640 HCAPLUS
- (55) Zarour, H; Cancer Res 2000, V60, P4946 HCAPLUS
- (56) Zarour, H; Proc Natl Acad Sci USA 2000, V97, P400 HCAPLUS
- L40 ANSWER 21 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2003:463217 HCAPLUS
- DN 139:177781
- ED Entered STN: 17 Jun 2003
- TI EphA2 Overexpression Decreases Estrogen Dependence and Tamoxifen Sensitivity
- AU Lu, Ming; Miller, Kathy D.; Gokmen-Polar, Yesim; Jeng, Meei-Huey; Kinch, Michael S.
- CS Department of Basic Medical Sciences, Purdue University Cancer Center, West Lafayette, IN, 47907, USA
- SO Cancer Research (2003), 63(12), 3425-3429 CODEN: CNREA8; ISSN: 0008-5472
- PB American Association for Cancer Research
- DT Journal
- LA English
- CC 14-1 (Mammalian Pathological Biochemistry) Section cross-reference(s): 2
- AB The EphA2 receptor tyrosine kinase is found at low levels on non-transformed adult breast epithelial cells but is frequently overexpressed on aggressive breast cancer cells. Recent studies have documented an inverse relationship between EphA2 and estrogen receptor expression in breast cancer cell lines. In our present study, we demonstrate that overexpression of EphA2 decreases estrogen dependence as defined using both in vitro and in vivo The EphA2-transfected cells demonstrate increased criteria. growth in vitro and form larger and more aggressive tumors in vivo. EphA2 overexpression also decreases the ability of tamoxifen to inhibit breast cancer cell growth and tumorigenesis. These effects of EphA2 overexpression can be overcome by antibody-based targeting of EphA2. In particular, certain EphA2 antibodies can resensitize EphA2-overexpressing breast tumor cells to tamoxifen. These results have important implications for understanding the mol. basis underlying estrogen dependence and provide further evidence that EphA2 may provide a much-needed therapeutic target for breast cancer.
- ST overexpression EphA2 decrease estrogen dependence tamoxifen sensitivity breast cancer
- IT Transformation, neoplastic
 - (EphA2 overexpression also decreases the ability of tamoxifen

to inhibit breast cancer cell growth and tumorigenesis) IT Human (EphA2 overexpression decreases estrogen dependence and tamoxifen sensitivity in human MCF-7 cell line) IT RL: BSU (Biological study, unclassified); BIOL (Biological study) (EphA2 overexpression decreases estrogen dependence and tamoxifen sensitivity in human MCF-7 cell line) IT Estrogen receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (Recent studies have documented an inverse relationship between EphA2 and estrogen receptor expression in breast cancer cell lines) IT Mammary gland (epithelium; EphA2 receptor tyrosine kinase is found at low levels on non-transformed adult breast epithelial cells but is frequently overexpressed on aggressive breast cancer cells) IT Mammary gland, neoplasm (human breast carcinoma MCF-7 cell line; EphA2 overexpression decreases estrogen dependence and tamoxifen sensitivity in human MCF-7 cell line) IT Cell proliferation (inhibition; EphA2 overexpression also decreases the ability of tamoxifen to inhibit breast cancer cell growth and tumorigenesis) IT Epithelium (mammary; EphA2 receptor tyrosine kinase is found at low levels on non-transformed adult breast epithelial cells but is frequently overexpressed on aggressive breast cancer cells) IT Drug targets (these results provide further evidence that EphA2 may provide a much-needed therapeutic target for breast cancer) TT 10540-29-1, Tamoxifen 149433-91-0, EphA2 receptor tyrosine kinase RL: BSU (Biological study, unclassified); BIOL (Biological study) (EphA2 overexpression decreases estrogen dependence and tamoxifen sensitivity in human MCF-7 cell line) RE.CNT THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD RE (1) Andres, A; Int J Cancer 1995, V63, P288 HCAPLUS (2) Carles-Kinch, K; Cancer Res 2002, V62, P2840 HCAPLUS (3) Dickson, R; Endocr Rev 1995, V16, P559 HCAPLUS (4) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS (5) Hulka, B; Cancer (Phila) 1994, V74, P1111 MEDLINE (6) Katzenellenbogen, B; Biol Reprod 1996, V54, P287 HCAPLUS (7) Katzenellenbogen, B; J Steroid Biochem Mol Biol 2000, V74, P279 HCAPLUS (8) Landis, S; CA Cancer J Clin 2001, V49, P8 (9) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS (10) MacGregor, J; Pharmacol Rev 1998, V50, P151 HCAPLUS (11) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS (12) Nakshatri, H; Mol Cell Biol 1997, V17, P3629 HCAPLUS (13) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS (14) Price, J; Breast Cancer Res Treat 1996, V39, P93 MEDLINE (15) Rochefort, H; CIBA Found Symp 1995, V191, P254 HCAPLUS (16) Woodhouse, E; Cancer (Phila) 1997, V80, P1529 MEDLINE (17) Zajchowski, D; Cancer Res 1993, V53, P5004 HCAPLUS (18) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS (19) Zantek, N; Clin Cancer Res 2001, V7, P3640 HCAPLUS

(20) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS

- haddad 10 / 823259 (21) Zelinski, D; J Cell Biochem 2002, V85, P714 HCAPLUS T.4 0 ANSWER 22 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN AN 2003:303553 HCAPLUS DN 139:50696 ED Entered STN: 21 Apr 2003 Differential regulation of EphA2 in normal and malignant cells ΤI ΑU Walker-Daniels, Jennifer; Hess, Angela R.; Hendrix, Mary J. C.; Kinch, Michael S. CS Department of Basic Medical Sciences, Purdue University Cancer Center, West Lafayette, IN, USA SO American Journal of Pathology (2003), 162(4), 1037-1042 CODEN: AJPAA4; ISSN: 0002-9440 PΒ American Society for Investigative Pathology DTJournal; General Review LA English CC 14-0 (Mammalian Pathological Biochemistry) A review on the biochem. and cellular consequences of EphA2 AB stimulation, especially in malignant cells. The mechanisms that may explain the overexpression and functional alterations of EphA2 in cancer are discussed. A hypothetical model representing a potential signaling pathway initiated by EphA2 and critical for vasculogenic mimicry is also presented. ST review EphA2 receptor tyrosine kinase signaling cancer TΤ Neoplasm Signal transduction, biological (differential regulation of EphA2 in cancer) TΤ 149433-91-0, EphA2 receptor tyrosine kinase RL: BSU (Biological study, unclassified); BIOL (Biological study) (differential regulation of EphA2 in cancer) THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Andres, A; Int J Cancer 1995, V63, P288 HCAPLUS (2) Andres, A; Oncogene 1994, V9, P1461 HCAPLUS (3) Bartley, T; Nature 1994, V368, P558 HCAPLUS (4) Belsches-Jablonski, A; Oncogene 2001, V20, P1465 HCAPLUS (5) Binnis, K; Mol Cell Biol 2000, V20, P4791 (6) Birchmeier, W; Curr Top Microbiol Immunol 1996, V213, P117 HCAPLUS (7) Biscardi, J; Mol Carcinog 1998, V21, P261 HCAPLUS (8) Bruckner, K; Curr Opin Neurobiol 1998, V8, P375 HCAPLUS (9) Carles-Kinch, K; Cancer Res 2001, V62, P2840 (10) Carpenter, G; Bioessays 2000, V22, P697 HCAPLUS (11) Ciossek, T; Eur J Neurosci 1998, V10, P1574 MEDLINE (12) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS (13) Dohn, M; Oncogene 2001, V20, P6503 HCAPLUS (14) Drescher, U; Curr Opin Neurobiol 1997, V7, P75 HCAPLUS (15) D'Amico, T; Ann Thorac Surg 2001, V72, P1144 MEDLINE (16) Easty, D; Melanoma Res 2000, V10, P401 HCAPLUS (17) Flanagan, J; Annu Rev Neurosci 1998, V21, P309 HCAPLUS
- (18) Flanagan, J; Cell 1997, V90, P403 HCAPLUS
- (19) Folkman, J; EXS 1997, V79, P1 MEDLINE
- (20) Gale, N; Cell Tissue Res 1997, V290, P227 HCAPLUS
- (21) Gale, N; Neuron 1996, V17, P9 HCAPLUS
- (22) Ganju, P; Oncogene 1994, V9, P1613 HCAPLUS
- (23) Geiger, B; Cold Spring Harb Symp Quant Biol 1992, V57, P631 HCAPLUS
- (24) Greene, M; Cancer 1999, V86, P2464 MEDLINE
- (25) Hainaut, P; Adv Cancer Res 2000, V77, P81 HCAPLUS

- (26) Hendrix, M; Cancer Res 2002, V62, P665 HCAPLUS
- (27) Hendrix, M; Proc Natl Acad Sci USA 2001, V98, P8018 HCAPLUS
- (28) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS
- (29) Hess, A; Proc Am Assoc Cancer Res 2002, V43, P36
- (30) Himanen, J; Nature 1998, V396, P486 HCAPLUS
- (31) Hock, B; Oncogene 1998, V17, P255 HCAPLUS
- (32) Hock, B; Proc Natl Acad Sci USA 1998, V95, P9779 HCAPLUS
- (33) Holland, S; Curr Opin Neurobiol 1998, V8, P117 HCAPLUS
- (34) Igney, F; Nature Rev, Cancer 2002, V2, P277 HCAPLUS
- (35) Joazeiro, C; Science 1999, V286, P309 HCAPLUS
- (36) Kikawa, K; J Biol Chem 2002, V277, P39274 HCAPLUS
- (37) Kinch, M; Biochem Soc Trans 1995, V23, P446 HCAPLUS
- (38) Klapper, L; Cancer Res 2000, V60, P3384 HCAPLUS
- (39) Koolpe, M; J Biol Chem 2002, V277, P46974 HCAPLUS
- (40) Labrador, J; EMBO J 1997, V16, P3889 HCAPLUS
- (41) Lackmann, M; J Biol Chem 1998, V273, P20228 HCAPLUS
- (42) Levkowitz, G; Genes Dev 1998, V12, P3663 HCAPLUS
- (43) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
- (44) Maniotis, A; Am J Pathol 1999, V155, P739 MEDLINE
- (45) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
- (46) Miao, H; Nat Cell Biol 2001, V3, P527 HCAPLUS
- (47) Nelson, M; Surg Clin N Am 1996, V76, P1257 MEDLINE
- (48) Nwosu, V; Hum Mol Genet 2001, V10, P2313 HCAPLUS
- (49) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
- (50) Orioli, D; Trends Genet 1997, V13, P354 HCAPLUS
- (51) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS
- (52) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS
- (53) Pandey, A; Science 1995, V268, P567 HCAPLUS
- (54) Pejovic, T; Ann Med 1995, V27, P73 MEDLINE
- (55) Pratt, R; Oncogene 2002, V21, P7690 HCAPLUS
- (56) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
- (57) Seftor, E; Clin Exp Metastasis 2002, V19, P233 HCAPLUS
- (58) Shirakawa, K; Cancer Res 2002, V62, P560 HCAPLUS
- (59) Shirakawa, K; Int J Cancer 2002, V99, P821 HCAPLUS
- (60) Stapleton, D; Nat Struct Biol 1999, V6, P44 HCAPLUS
- (61) Sulman, E; Genomics 1997, V40, P371 HCAPLUS
- (62) Thanos, C; Science 1999, V283, P833 HCAPLUS
- (63) Vousden, K; Biochim Biophys Acta 2002, V1602, P47 HCAPLUS
- (64) Walker-Daniels, J; Mol Cancer Res 2002, V1, P79 HCAPLUS
- (65) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
- (66) Waterman, H; EMBO J 2002, V21, P303 HCAPLUS
- (67) Wong, A; Proc Natl Acad Sci USA 2002, V99, P6684 HCAPLUS
- (68) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
- (69) Zantek, N; Clin Cancer Res 2001, V7, P3640 HCAPLUS
- (70) Zantek, N; J Cell Physiol 2001
- (71) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
- (72) Zetter, B; Semin Cancer Biol 1993, V4, P219 HCAPLUS
- (73) Zhou, R; Pharmacol Ther 1998, V77, P151 HCAPLUS
- (74) Zisch, A; Cell Tissue Res 1997, V290, P217 HCAPLUS
- L40 ANSWER 23 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2003:141172 HCAPLUS
- DN 139:82846
- ED Entered STN: 25 Feb 2003
- TI Overexpression and functional alterations of the EphA2 tyrosine kinase in cancer
- AU Kinch, Michael S.; Carles-Kinch, Kelly
- CS MedImmune, Inc., Gaithersburg, MD, USA
- SO Clinical & Experimental Metastasis (2003), 20(1), 59-68 CODEN: CEXMD2; ISSN: 0262-0898

```
PB
     Kluwer Academic Publishers
DT
     Journal
LA
     English
CC
     14-1 (Mammalian Pathological Biochemistry)
     Cancer is a disease of aberrant signal transduction. The expression and
AB
     function of intracellular signaling pathways are frequently subverted as
     cells progress towards a metastatic phenotype. In particular,
     tyrosine kinases initiate powerful signals that govern
     many different aspects of cell behavior. In Recent studies have
     demonstrated that the EphA2 receptor tyrosine
     kinase is frequently overexpressed and functionally altered in
     aggressive tumor cells, and that these changes promote metastatic
     character. Herein, we provide an overview of our current understanding of
     EphA2, with emphasis upon the differential regulation of
     EphA2 expression and function. We also show that differential
     EphA2 expression and function may provide a unique opportunity for
     selective therapeutic targeting of EphA2 in metastatic disease.
ST
     EphA2 receptor tyrosine kinase
     intracellular signaling cancer
TΤ
     Neoplasm
     Second messenger system
     Signal transduction, biological
        (overexpression and functional alterations of EphA2
        tyrosine kinase in cancer)
TT
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (overexpression and functional alterations of EphA2
        tyrosine kinase in cancer)
RE.CNT
              THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD
       92
(1) Andres, A; Int J Cancer 1995, V63, P288 HCAPLUS
(2) Andres, A; Oncogene 1994, V9, P1461 HCAPLUS
(3) Bartley, T; Nature 1994, V368, P558 HCAPLUS
(4) Berclaz, G; Biochem Biophys Res Commun 1996, V226, P869 HCAPLUS
(5) Birchmeier, C; Acta Anatomica 1996, V156, P217 MEDLINE
(6) Birchmeier, W; Curr Top Microbiol Immunol 1996, V213, P117 HCAPLUS
(7) Bissell, M; Am J Pathol 1999, V155, P675 MEDLINE
(8) Blume-Jensen, P; Nature 2001, V411, P355 HCAPLUS
(9) Bovenkamp, D; Dev Dynam 1997, V209, P166 HCAPLUS
(10) Carles-Kinch, K; Cancer Res 2001, V62, P2840
(11) Carter, P; Nat Rev Cancer 2001, V1, P118 HCAPLUS
(12) Cates, C; Cancer Lett 1996, V110, P49 HCAPLUS
(13) Chen, J; J Biol Chem 1998, V273, P24670 HCAPLUS
(14) Chen, J; Oncogene 1996, V12, P979 HCAPLUS
(15) Clark, E; J Cell Biol 1998, V142, P573 HCAPLUS
(16) Connor, R; Dev Biol 1998, V193, P21 HCAPLUS
(17) Davis, S; Science 1994, V266, P816 HCAPLUS
(18) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS
(19) Dohn, M; Oncogene 2001, V20, P6503 HCAPLUS
(20) Easty, D; Cancer Res 2000, V55, P2528
(21) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
(22) Easty, D; Melanoma Res 2000, V10, P401 HCAPLUS
(23) Fagotto, F; Dev Biol 1996, V180, P445 HCAPLUS
(24) Fidler, I; Cancer: Principles and Practice of Oncology, 5th ed 1997, P135
(25) Flanagan, J; Cell 1997, V90, P403 HCAPLUS
(26) Folkman, J; EXS 1997, V79, P1 MEDLINE
(27) Frisch, S; Curr Opin Cell Biol 1997, V9, P701 HCAPLUS
(28) Gale, N; Cell Tissue Res 1997, V290, P227 HCAPLUS
(29) Gale, N; Neuron 1996, V17, P9 HCAPLUS
```

- haddad 10 / 823259 (30) Ganju, P; Oncogene 1994, V9, P1613 HCAPLUS (31) Geiger, B; Annu Rev Cell Biol 1992, V8, P307 HCAPLUS (32) Giancotti, F; Science 1999, V285, P1028 HCAPLUS (33) Helbling, P; Mech Dev 1998, V78, P63 HCAPLUS (34) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS (35) Holland, S; Curr Opin Neurobiol 1998, V8, P117 HCAPLUS (36) Hunter, T; Cold Spring Harbor Symp Quant Biol 1992, V57, P25 HCAPLUS (37) Hunter, T; Phil Trans R Soc London Ser B Biol Sci 1998, V353, P583 HCAPLUS (38) Jove, J; Annu Rev Cell Biol 1987, V3, P31 (39) Kinch, M; Biochem Soc Trans 1995, V23, P446 HCAPLUS (40) Kinch, M; Hybridoma 1998, V17, P227 HCAPLUS (41) Kinch, M; J Cell Biol 1995, V130, P461 HCAPLUS (42) Lawrence, J; World J Urol 1996, V14, P124 MEDLINE (43) Lemke, G; Mol Cell Neurosci 1997, V9, P331 HCAPLUS (44) Lickliter, J; PNAS 1996, V93, P145 HCAPLUS (45) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS (46) Magal, E; J Neurosci Res 1996, V43, P735 HCAPLUS (47) Maniotis, A; Am J Pathol 1999, V155, P739 MEDLINE (48) Marcus, R; Dev Biol 1996, V180, P786 HCAPLUS (49) McCawley, L; Mol Med Today 2000, V6, P149 HCAPLUS (50) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS (51) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS (52) Miao, H; Nat Cell Biol 2001, V3, P527 HCAPLUS (53) Mori, T; Brain Res 1995, V29, P325 HCAPLUS (54) Naruse-Nakajima, C; Mech Dev 2001, V102, P95 HCAPLUS (55) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS (56) Orioli, D; Trends Genet 1997, V13, P354 HCAPLUS (57) Orsulic, S; J Cell Sci 2000, V113, P1793 HCAPLUS (58) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS (59) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS (60) Pandey, A; Science 1995, V268, P567 HCAPLUS (61) Parise, L; Semin Cancer Biol 2000, V10, P407 HCAPLUS (62) Parsons, J; Oncogene 2000, V19, P5606 HCAPLUS (63) Pasquale, E; Curr Opin Cell Biol 1997, V9, P608 HCAPLUS (64) Patstone, G; Growth Factors 1993, V9, P243 MEDLINE (65) Pawson, T; Nature 1995, V373, P573 HCAPLUS (66) Pawson, T; Science 1997, V278, P2075 HCAPLUS (67) Potla, L; Cancer Lett 2002, V175, P187 HCAPLUS (68) Pratt, R; Oncogene, In Press 2002 (69) Price, J; In Vivo 1994, V8, P145 MEDLINE (70) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS (71) Ruoslahti, E; Adv Cancer Res 1999, V76, P1 HCAPLUS (72) Ruoslahti, E; Sci Am 1996, V275, P72 HCAPLUS (73) Schoenwaelder, S; Curr Opin Cell Biol 1999, V11, P274 HCAPLUS (74) Sefton, M; Dev Biol 1997, V188, P363 HCAPLUS (75) Shao, H; J Biol Chem 1995, V270, P5636 HCAPLUS (76) Sternlicht, M; Annu Rev Cell Dev Biol 2001, V17, P463 HCAPLUS (77) Tessier-Lavigne, M; Cell 1995, V82, P345 HCAPLUS (78) van der Geer, P; Trends Biochem Sci 1995, V20, P277 HCAPLUS (79) Vleminckx, K; Bioessays 1999, V21, P211 MEDLINE (80) Volberg, T; EMBO J 1992, V11, P1733 HCAPLUS
- (81) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
- (82) Wang, H; Neuron 1997, V18, P383 HCAPLUS
- (83) Weinstein, D; Mech Dev 1996, V57, P133 HCAPLUS
- (84) Welch, D; Breast Cancer Res 2000, V2, P408 HCAPLUS
- (85) Wieser, R; Environ Health Perspect 1990, V88, P251 MEDLINE
- (86) Yamada, K; Curr Opin Cell Biol 1997, V9, P76 HCAPLUS
- (87) Yap, A; Ann Rev Cell Dev Biol 1997, V13, P119 HCAPLUS
- (88) Zantek, N; Cell Growth Differentiation 1999, V10, P629 HCAPLUS
- (89) Zantek, N; Clin Cancer Res 2001, V7, P3640 HCAPLUS

```
(90) Zantek, N; J Cell Physiol 2001
(91) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
(92) Zetter, B; Semin Cancer Biol 1993, V4, P219 HCAPLUS
    ANSWER 24 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2003:106711 HCAPLUS
DN
     138:335310
     Entered STN: 11 Feb 2003
ED
     Predictive value of the EphA2 receptor
TT
     tyrosine kinase in lung cancer recurrence and survival
ΑU
     Kinch, Michael S.; Moore, Mary-Beth; Harpole, David H., Jr.
CS
     MedImmune, Inc., Gaithersburg, MD, 20878, USA
     Clinical Cancer Research (2003), 9(2), 613-618
SO
     CODEN: CCREF4; ISSN: 1078-0432
     American Association for Cancer Research
PB
DT
     Journal
LΑ
     English
CC
     14-1 (Mammalian Pathological Biochemistry)
     PURPOSE: Underestimation of disease severity is a major problem
AB
     confronting the successful clin. management of non-small cell lung cancer.
     Recent advances in mol. biol. substaging may provide an opportunity to
     identify those patients with the most aggressive forms of the disease, but
     there is a continuing need for accurate markers of disease relapse and
     survival. Exptl. Design: In the authors' present study, immunohistochem.
     analyses of a retrospective database of pathol. specimens were used to
     demonstrate that the EphA2 receptor kinase
     is frequently overexpressed in NSCLC. RESULTS: Initial presentation with
     high levels of EphA2 predicts subsequent survival, overall
     relapse, and site of relapse. Specifically, high levels of EphA2
     in the primary tumor predict brain metastases, whereas low levels of
     EphA2 relate to disease-free survival or contralateral lung
     metastasis. CONCLUSIONS: These data suggest that EphA2 may
     provide a mol. marker to identify and predict patients who have isolated
     brain metastases. Moreover, the high levels of EphA2 in lung
     cancer may provide an opportunity for therapeutic targeting.
ST
     lung cancer EphA2 receptor tyrosine
     kinase
IT
     Brain, neoplasm
     Lung, neoplasm
        (metastasis; predictive value of the EphA2 receptor
        tyrosine kinase in lung cancer recurrence and
        survival)
TΤ
     Lung, neoplasm
        (non-small-cell carcinoma; predictive value of the EphA2
        receptor tyrosine kinase in lung cancer
        recurrence and survival)
IT
     Human
        (predictive value of the EphA2 receptor
        tyrosine kinase in lung cancer recurrence and
        survival)
IT
     Carcinoma
        (pulmonary non-small-cell; predictive value of the EphA2
        receptor tyrosine kinase in lung cancer
        recurrence and survival)
TΤ
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (predictive value of the EphA2 receptor
        tyrosine kinase in lung cancer recurrence and
        survival)
```

```
RE.CNT 29
              THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Andres, A; Int J Cancer 1995, V63, P288 HCAPLUS
(2) Andres, A; Oncogene 1994, V9, P1461 HCAPLUS
(3) Carles-Kinch, K; Cancer Res 2001, V62, P2840
(4) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS
(5) Dohn, M; Oncogene 2001, V20, P6503 HCAPLUS
(6) D'Amico, T; Ann Thorac Surg 2001, V72, P1144 MEDLINE
(7) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
(8) Easty, D; Melanoma Res 2000, V10, P401 HCAPLUS
(9) Figlin, R; N Engl J Med 1988, V318, P1300 MEDLINE
(10) Gale, N; Cell Tissue Res 1997, V290, P227 HCAPLUS
(11) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS
(12) Landis, S; CA - Cancer J Clin 1999, V49, P8 MEDLINE
(13) Lau, C; Chest Surg Clin N Am 2000, V10, P781 MEDLINE
(14) Lopez-Encuentra, A; Lung Cancer 2000, V29, P79 MEDLINE
(15) Magilligan, D; Ann Thorac Surg 1986, V42, P360
(16) Mountain, C; Chest Surg Clin N Am 2000, V10, P83 MEDLINE
(17) Mountain, C; Semin Surg Oncol 2000, V18, P106 MEDLINE
(18) Nesbitt, J; Ann Thorac Surg 1995, V60, P466 MEDLINE
(19) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
(20) Pandey, A; Curr Biol 1995, V5, P986 HCAPLUS
(21) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
(22) Sidransky, D; Nat Rev Cancer 2002, V2, P210 HCAPLUS
(23) Thomas, P; Ann Thorac Surg 1990, V49, P242 MEDLINE
(24) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
(25) Wiest, J; J Cell Biochem Suppl 1997, V28-29, P64 MEDLINE
(26) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
(27) Zantek, N; Clin Cancer Res 2001, V7, P3640 HCAPLUS
(28) Zantek, N; J Cell Physiol 2001, V85, P714
(29) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
     ANSWER 25 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
L40
AN
     2003:61644 HCAPLUS
DN
     138:252693
     Entered STN: 27 Jan 2003
ED
     EphA2 overexpression correlates with poor prognosis in
TI
     esophageal squamous cell carcinoma
ΑU
     Miyazaki, Tatsuya; Kato, Hiroyuki; Fukuchi, Minoru; Nakajima, Masanobu;
     Kuwano, Hiroyuki
     Department of Surgery I, Gunma University Faculty of Medicine, Gunma,
CS
     371-8511, Japan
     International Journal of Cancer (2003), 103(5), 657-663
SO
     CODEN: IJCNAW; ISSN: 0020-7136
PB
     Wiley-Liss, Inc.
DT
     Journal
LA
     English
CC
     14-1 (Mammalian Pathological Biochemistry)
     EphA2 is a member of the Eph family of
AB
     receptor tyrosine kinases, which interact with
     cell-bound ligands known as ephrins. EphA2 expression
     was investigated by immunohistochem. with an anti-EphA2
     monoclonal antibody in 80 patients with esophageal squamous cell carcinoma
     (ESCC) who had undergone surgery. EphA2 overexpression was pos.
     in 40 of the 80 patients (50%). A significant correlation was observed
     between EphA2 expression and regional lymph node metastasis
     (p=0.023), number of lymph node metastases (p=0.011) and poor degree of tumor
     differentiation (p=0.004). The survival rates of EphA2-pos.
     patients were poorer than those of EphA2-neg. patients
     (p=0.014). The 5-yr survival rate of patients without EphA2
```

haddad - 10 / 823259 overexpression was 68%, whereas that of patients with EphA2 overexpression was 29%. EphA2 expression was also investigated in 7 ESCC cell lines (TE-1, -2, -8, -13, -15, TT and TTn) and 1 immortalized human esophageal keratinocyte cell line (CHEK-1). blotting revealed different levels of EphA2 expression in the 8 cell lines. EphA2 was expressed at a high level in the ESCC cell lines compared to CHEK-1. EphA2 phosphorylation was demonstrated in all cell lines. Northern blot anal. showed that EphA2 mRNA expression in TE-1 was greater than that in the other ESCC cell lines. The observation of small gaps on Western blot anal. of the ESCC cell lines suggests that there may be a mechanism for EphA2 regulation at the point of translation. In conclusion, EphA2 overexpression appears to be related to poor degree of tumor differentiation and lymph node metastasis in ESCC. Consequently, patients with EphA2 overexpression have a poorer prognosis than those without. EphA2 is a potential target to prevent ESCC cells spreading into the lymphatic drainage. EphA2 esophagus carcinoma prognosis Human Prognosis (EphA2 overexpression correlates with poor prognosis in esophageal squamous cell carcinoma) RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study) (ephrin, A2; EphA2 overexpression correlates with poor prognosis in esophageal squamous cell carcinoma) Carcinoma (esophageal squamous cell; EphA2 overexpression correlates with poor prognosis in esophageal squamous cell carcinoma) Phosphorylation, biological (receptor, of EphA2; EphA2 overexpression correlates with poor prognosis in esophageal squamous cell carcinoma) Esophagus, neoplasm (squamous cell carcinoma; EphA2 overexpression correlates with poor prognosis in esophageal squamous cell carcinoma) 149433-91-0, EphA2 receptor tyrosine kinase RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study) (EphA2 overexpression correlates with poor prognosis in esophageal squamous cell carcinoma) THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT (1) Altorki, N; Ann Surg 2001, V234, P581 MEDLINE (2) Ando, N; J Thorac Cardiovasc Surg 1997, V114, P205 MEDLINE (3) Berrino, F; Survival of cancer patients in Europe-the Eurocare Study 1995 (4) Carter, N; Nat Cell Biol 2002, V4, P565 HCAPLUS (5) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS

- (6) Easty, D; Cancer Res 1995, V55, P2528 HCAPLUS
- (7) Frisen, J; EMBO J 1999, V18, P5159 HCAPLUS
- (8) Gale, N; Neuron 1996, V17, P9 HCAPLUS

ST

IT

IT

IT

IT

IT

IT

RE

- (9) Kopreski, M; Anticancer Res 1996, V16, P3037 MEDLINE
- (10) Kuwano, H; Hepato-gastroenterol 1997, V44, P170 MEDLINE
- (11) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
- (12) Mellitzer, G; Nature 1999, V400, P77 HCAPLUS
- (13) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
- (14) Miao, H; Nat Cell Biol 2001, V3, P527 HCAPLUS
- (15) Munoz, N; Eur J Gastroenterol Hepatol 1994, V6, P649
- (16) Nishihira, T; J Cancer Res Clin Oncol 1993, V119, P441 HCAPLUS

- (17) Orsulic, S; J Cell Sci 2000, V113, P1793 HCAPLUS (18) Parkin, D; Int J Cancer 1993, V54, P594 MEDLINE (19) Pisani, P; Int J Cancer 1993, V55, P891 MEDLINE (20) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS (21) Sashiyama, H; Cancer Lett 2002, V177, P21 HCAPLUS (22) van der Geer, P; Annu Rev Cell Biol 1994, V10, P251 HCAPLUS (23) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS (24) Weiner, L; Semin Oncol 1999, V26, P43 HCAPLUS (25) Xu, Q; J Mol Med 1997, V75, P576 HCAPLUS (26) Xu, Q; Nature 1999, V399, P267 HCAPLUS (27) Zantek, N; Cell Growth Diff 1999, V10, P629 HCAPLUS (28) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS ANSWER 26 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN 2002:968922 HCAPLUS AΝ DN 138:167753 Entered STN: 23 Dec 2002 ED c-Cbl-dependent EphA2 protein degradation is induced by ligand binding Walker-Daniels, Jennifer; Riese, David J., II; Kinch, Michael S. ΑU Department of Basic Medical Sciences, Purdue University Cancer Center, CS West Lafayette, IN, USA SO Molecular Cancer Research (2002), 1(1), 79-87 CODEN: MCROC5; ISSN: 1541-7786 PB American Association for Cancer Research DT Journal LA English CC 14-1 (Mammalian Pathological Biochemistry) Section cross-reference(s): 2 AB The EphA2 receptor protein tyrosine kinase is overexpressed and functionally altered in a large number of human carcinomas. Despite its elevated levels in cancer, the EphA2 on the surface of malignant cells demonstrates lower levels of ligand binding and tyrosine phosphorylation than the EphA2 on non-transformed epithelial cells. In our present study, we demonstrate that ligand-mediated stimulation causes EphA2 to be internalized and degraded. The mechanism of this response involves ligand-mediated autophosphorylation of EphA2, which promotes an association between EphA2 and the c-Cbl adaptor protein. We also show that c-Cbl promotes stimulation-dependent EphA2 degradation These findings are important for understanding the causes of EphA2 overexpression in malignant cells and provide a foundation for investigating EphA2 as a potential target for therapeutic intervention. EphA2 receptor tyrosine kinase STdegrdn Cbl protein breast carcinoma; ephrin A1 EphA2 membrane internalization autophosphorylation prostate carcinoma Cell membrane IT (EphA2 associated with; c-Cbl-dependent EphA2 protein degradation is induced by ligand binding in invasive human breast carcinoma and prostate carcinoma cells) IT Phosphorylation, biological (autophosphorylation, of EphA2; c-Cbl-dependent EphA2 protein degradation is induced by ligand binding in invasive human
- IT Molecular association (c-Cbl EphA2; c-Cbl-dependent EphA2

breast carcinoma and prostate carcinoma cells)

protein degradation is induced by ligand binding in invasive human breast carcinoma and prostate carcinoma cells)

```
IT Human
```

Protein degradation

(c-Cbl-dependent **EphA2 protein** degradation is induced by ligand binding in invasive human breast carcinoma and prostate carcinoma cells)

IT Mammary gland, neoplasm

Prostate gland, neoplasm

carcinoma cells)

(carcinoma; c-Cbl-dependent **EphA2 protein** degradation is induced by ligand binding in invasive human breast carcinoma and prostate carcinoma cells)

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (ephrin, ephrin-A1, EphA2 ligand;
 c-Cbl-dependent EphA2 protein degradation is induced by
 ligand binding in invasive human breast carcinoma and prostate

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (gene c-Cbl; c-Cbl-dependent **EphA2 protein** degradation is induced by ligand binding in invasive human breast carcinoma and prostate carcinoma cells)

IT Biological transport

(internalization, of **EphA2**; c-Cbl-dependent **EphA2 protein** degradation is induced by ligand binding in invasive human breast carcinoma and prostate carcinoma cells)

IT Carcinoma

(mammary; c-Cbl-dependent **EphA2 protein** degradation is induced by ligand binding in invasive human breast carcinoma and prostate carcinoma cells)

IT Carcinoma

(prostatic; c-Cbl-dependent **EphA2** protein degradation is induced by ligand binding in invasive human breast carcinoma and prostate carcinoma cells)

IT 149433-91-0, EphA2 receptor tyrosine kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (c-Cbl-dependent **EphA2 protein** degradation is induced by ligand binding in invasive human breast carcinoma and prostate carcinoma cells)

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Andoniou, C; EMBO J 1994, V13, P4515 HCAPLUS
- (2) Bae, S; Breast Cancer Res Treat 1993, V24, P241 MEDLINE
- (3) Bartley, T; Nature 1994, V368, P558 HCAPLUS
- (4) Baselga, J; Cancer Res 1998, V58, P2825 HCAPLUS
- (5) Birchmeier, W; BioEssays 1995, V17, P97 HCAPLUS
- (6) Carles-Kinch, K; Cancer Res 2002, V62, P2840 HCAPLUS
- (7) Carpenter, G; BioEssays 2000, V22, P697 HCAPLUS
- (8) Carpenter, G; J Biol Chem 1990, V265, P7709 HCAPLUS
- (9) Davis, S; Science 1994, V266, P816 HCAPLUS
- (10) de Jong, R; J Biol Chem 1995, V270, P21468 HCAPLUS
- (11) Dickson, R; Breast Cancer Res Treat 1996, V38, P1 MEDLINE
- (12) Easty, D; Cancer Res 1995, V55, P2528 HCAPLUS
- (13) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
- (14) Feshchenko, E; J Biol Chem 1998, V273, P8323 HCAPLUS
- (15) Gale, N; Cell Tissue Res 1997, V290, P227 HCAPLUS
- (16) Garcia-Guzman, M; Oncogene 2000, V19, P4058 HCAPLUS
- (17) Jain, S; Oncogene 1997, V14, P2217 HCAPLUS
- (18) Joazeiro, C; Science 1999, V286, P309 HCAPLUS
- (19) Kim, H; Histol Histopathol 1999, V14, P1175 HCAPLUS

- (20) Kinch, M; Biochem Soc Trans 1995, V23, P446 HCAPLUS
- (21) Kinch, M; Hybridoma 1998, V17, P227 HCAPLUS
- (22) Kinch, M; J Cell Biol 1995, V130, P461 HCAPLUS
- (23) Klapper, L; Cancer Res 2000, V60, P3384 HCAPLUS
- (24) Kolibaba, K; Biochim Biophys Acta 1997, V1333, PF217 HCAPLUS
- (25) Langdon, W; Aust N Z J Med 1995, V25, P859 MEDLINE
- (26) Langdon, W; Proc Natl Acad Sci USA 1989, V86, P1168 HCAPLUS
- (27) Levitzki, A; Science 1995, V267, P1782 HCAPLUS
- (28) Levkowitz, G; Mol Cell 1999, V4, P1029 HCAPLUS
- (29) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
- (30) Magal, E; J Neurosci Res 1996, V43, P735 HCAPLUS
- (31) Malitschek, B; BioEssays 1995, V17, P1017 HCAPLUS
- (32) Meng, W; Nature 1999, V398, P84 HCAPLUS
- (33) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
- (34) Miyake, S; Crit Rev Oncog 1997, V8, P189 HCAPLUS
- (35) Miyake, S; Proc Natl Acad Sci USA 1998, V95, P7927 HCAPLUS
- (36) Pandey, A; Curr Biol 1995, V5, P986 HCAPLUS
- (37) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS
- (38) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS
- (39) Pandey, A; Science 1995, V268, P567 HCAPLUS
- (40) Pasquale, E; Curr Opin Cell Biol 1997, V9, P608 HCAPLUS
- (41) Patarca, R; Crit Rev Oncog 1996, V7, P343 HCAPLUS
- (42) Press, M; Prog Clin Biol Res 1990, V354A, P209 MEDLINE
- (43) Rabin, R; Lab Invest 1995, V73, P311
- (44) Reese, D; Stem Cells 1997, V15, P1 HCAPLUS
- (45) Riese, D; Oncogene 1995, V10, P1431 HCAPLUS
- (46) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
- (47) Rusch, V; Cytokine Growth Factor Rev 1996, V7, P133 HCAPLUS
- (48) Shak, S; Semin Oncol 1999, V26, P71 HCAPLUS
- (49) Sorkin, A; J Biol Chem 1991, V266, P8355 HCAPLUS
- (50) Tanaka, S; Nature 1996, V383, P528 HCAPLUS
- (51) Thien, C; Oncogene 1997, V14, P2239 HCAPLUS
- (52) Ueno, H; J Biol Chem 1997, V272, P8739 HCAPLUS
- (53) van der Geer, P; Annu Rev Cell Biol 1994, V10, P251 HCAPLUS
- (54) Volberg, T; EMBO J 1992, V11, P1733 HCAPLUS
- (55) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
- (56) Wang, Y; J Biok Chem 1996, V271, P17 HCAPLUS (57) Waterman, H; J Biol Chem 1999, V274, P22151 HCAPLUS
- (58) Weiner, L; Semin Oncol 1999, V26, P43 HCAPLUS
- (59) Yokouchi, M; J Biol Chem 1999, V274, P31707 HCAPLUS
 (60) Yoon, C; Science 1995, V269, P1102 HCAPLUS
- (61) Zantek, N; Cell Growth & Differ 1999, P629 HCAPLUS
- (62) Zantek, N; Clin Cancer Res 2001, V7(11), P3640 HCAPLUS
- (63) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
- (64) Zetter, B; Semin Cancer Biol 1993, V4, P219 HCAPLUS
- L40 ANSWER 27 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2002:968915 HCAPLUS
- DN 138:215719
- ED Entered STN: 23 Dec 2002
- TI Blockade of EphA receptor tyrosine kinase activation inhibits vascular endothelial cell growth factor-induced angiogenesis
- AU Cheng, Nikki; Brantley, Dana M.; Liu, Hua; Lin, Qin; Enriquez, Miriam; Gale, Nick; Yancopoulos, George; Cerretti, Douglas Pat; Daniel, Thomas O.; Chen, Jin
- CS Department of Cancer Biology, Division of Rheumatology, Vanderbilt University School of Medicine, Nashville, TN, 37232, USA
- SO Molecular Cancer Research (2002), 1(1), 2-11 CODEN: MCROC5; ISSN: 1541-7786

```
PΒ
     American Association for Cancer Research
DT
     Journal
LA
     English
CC
     2-10 (Mammalian Hormones)
     Angiogenesis is a multistep process involving a diverse array of mol.
AB
     signals. Ligands for receptor tyrosine
     kinases (RTKs) have emerged as critical mediators of angiogenesis.
     Three families of ligands, vascular endothelial cell growth factors
     (VEGFs), angiopoietins, and ephrins, act via RTKs expressed in
     endothelial cells. Recent evidence indicates that VEGF cooperates with
     angiopoietins to regulate vascular remodeling and angiogenesis in both
     embryogenesis and tumor neovascularization. However, the relationship
     between VEGF and ephrins remains unclear. Here we show that
     interaction between EphA RTKs and ephrinA ligands is
     necessary for induction of maximal neovascularization by VEGF.
     EphA2 RTK is activated by VEGF through induction of
     ephrinAl ligand. A soluble EphA2-Fc receptor
     inhibits VEGF-, but not basic fibroblast growth factor-induced
     endothelial cell survival, migration, sprouting, and corneal angiogenesis.
     As an independent, but complementary approach, EphA2 antisense
     oligonucleotides inhibited endothelial expression of
     EphA2 receptor and suppressed ephrinA1- and
     VEGF-induced cell migration. Taken together, these data indicate an
     essential role for EphA receptor activation in
     VEGF-dependent angiogenesis and suggest a potential new target for
     therapeutic intervention in pathogenic angiogenesis.
ST
     EphA receptor tyrosine kinase VEGF
     ephrinAl vessel endothelium angiogenesis
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (EphrinA1; blockade of EphA
        receptor tyrosine kinase activation
        inhibits VEGF-induced endothelial cell survival, migration and
        angiogenesis)
IT
     Apoptosis
     Cell migration
     Cell proliferation
        (blockade of EphA receptor
        tyrosine kinase activation inhibits
        VEGF-induced endothelial cell survival, migration and angiogenesis)
TT
    Blood vessel
        (endothelium; blockade of EphA receptor
        tyrosine kinase activation inhibits
        VEGF-induced endothelial cell survival, migration and angiogenesis)
TΤ
     Angiogenesis
        (neovascularization; blockade of EphA
        receptor tyrosine kinase activation
        inhibits VEGF-induced endothelial cell survival, migration and
        angiogenesis)
     Phosphorylation, biological
IT
        (receptor; blockade of EphA
        receptor tyrosine kinase activation
        inhibits VEGF-induced endothelial cell survival, migration and
        angiogenesis)
ΤT
    Endothelium
        (vascular; blockade of EphA receptor
        tyrosine kinase activation inhibits
        VEGF-induced endothelial cell survival, migration and angiogenesis)
IT
     106096-93-9, Basic fibroblast growth factor
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
```

(blockade of EphA receptor

Entered STN: 02 Dec 2002

EphA2 Receptor

ED TI

```
tyrosine kinase activation inhibits VEGF-,
        but FGF-induced endothelial cell survival, migration and angiogenesis)
TT
     127464-60-2, Vascular endothelial growth factor 149433-91-0,
     EphA2 receptor tyrosine kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (blockade of EphA receptor
        tyrosine kinase activation inhibits
        VEGF-induced endothelial cell survival, migration and angiogenesis)
RE.CNT
              THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Adams, R; Genes Dev 1999, V3, P295
(2) Ades, E; J Invest Dermatol 1992, V99, P683 MEDLINE
(3) Asahara, T; Circ Res 1998, V83, P233 HCAPLUS
(4) Brantley, D; Oncogene 2002, V21, P7011 HCAPLUS
(5) Brekken, R; Cancer Res 2000, V60, P5117 HCAPLUS
(6) Bruckner, K; Science 1997, V275, P1640 MEDLINE
(7) Carmeliet, P; Nature 1996, V380, P435 HCAPLUS
(8) Chen, J; Oncogene 1996, V12, P979 HCAPLUS
(9) Cheng, N; Cytokine Growth Factor Rev 2002, V13, P75 HCAPLUS
(10) Daniel, T; Cancer Res 1999, V59, P4574 HCAPLUS
(11) Daniel, T; Kidney Int Suppl 1996, V57, PS73 HCAPLUS
(12) Davy, A; Genes Dev 1999, V13, P3125 HCAPLUS
(13) Drevs, J; Cancer Res 2000, V60, P4819 HCAPLUS
(14) Ferrara, N; Nature 1996, V380, P439 HCAPLUS
(15) Fong, G; Nature 1995, V376, P66 HCAPLUS
(16) Gale, N; Genes Dev 1999, V13, P1055 HCAPLUS
(17) Gerber, H; J Biol Chem 1998, V273, P30336 HCAPLUS
(18) Gerety, S; Mol Cell 1999, V4, P403 HCAPLUS
(19) Griffioen, A; Pharmacol Rev 2000, V52, P237 HCAPLUS
(20) Haigh, J; Development 2000, V127, P1445 HCAPLUS
(21) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS
(22) Holash, J; Science 1999, V284, P1994 HCAPLUS
(23) Holder, N; Development 1999, V126, P2033 HCAPLUS
(24) Holland, S; Nature 1996, V383, P722 HCAPLUS
(25) Holzman, L; Mol Cell Biol 1990, V10, P5830 HCAPLUS
(26) Huai, J; J Biol Chem 2001, V276, P6689 HCAPLUS
(27) Kenyon, B; Invest Ophthalmol Vis Sci 1996, V37, P1625 MEDLINE
(28) Kolizek, T; Curr Biol 1998, V8, P529
(29) Lin, P; Cell Growth & Differ 1998, V9, P49 HCAPLUS
(30) Maisonpierre, P; Science 1997, V277, P55 HCAPLUS
(31) McBride, J; Mech Dev 1998, V77, P201 HCAPLUS
(32) Miquerol, L; Development 2000, V127, P3941 HCAPLUS
(33) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
(34) Pandey, A; Science 1995, V268, P567 HCAPLUS
(35) Phillips, G; In Vivo 1994, V8, P961 HCAPLUS
(36) Rousseau, S; Oncogene 1997, V15, P2169 HCAPLUS
(37) Shalaby, F; Nature 1995, V376, P62 HCAPLUS
(38) Vajkoczy, P; Neoplasia 1999, V1, P31 HCAPLUS
(39) Vitaliti, A; Cancer Res 2000, V60, P4311 HCAPLUS
(40) Wang, H; Cell 1998, V93, P741 HCAPLUS
(41) Wood, J; Cancer Res 2000, V60, P2178 HCAPLUS
(42) Yancopoulos, G; Nature 2000, V407, P242 HCAPLUS
L40
    ANSWER 28 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
     2002:910729 HCAPLUS
ΔN
DN
     139:856
```

An Ephrin Mimetic Peptide That Selectively Targets the

```
ΑU
     Koolpe, Mitchell; Dail, Monique; Pasquale, Elena B.
CS
     Burnham Institute, La Jolla, CA, 92037, USA
SO
     Journal of Biological Chemistry (2002), 277(49), 46974-46979
     CODEN: JBCHA3; ISSN: 0021-9258
PB
     American Society for Biochemistry and Molecular Biology
DT
     Journal
LA
     English
CC
     1-12 (Pharmacology)
AB
     Eph receptor tyrosine kinases
     represent promising disease targets because they are differentially
     expressed in pathol. vs. normal tissues. The EphA2
     receptor is up-regulated in transformed cells and tumor
     vasculature where it likely contributes to cancer pathogenesis.
     exploit EphA2 as a therapeutic target, the authors used phage
     display to identify two related peptides that bind selectively to
     EphA2 with high affinity (submicromolar KD values). The peptides
     target the ligand-binding domain of EphA2 and compete with
     ephrin ligands for binding. Remarkably, one of the peptides has
     ephrin-like activity in that it stimulates EphA2
     tyrosine phosphorylation and signaling. Furthermore, this peptide
     can deliver phage particles to endothelial and tumor cells expressing
     EphA2. In contrast, peptides corresponding to receptor
     -interacting portions of ephrin ligands bind weakly and
     promiscuously to many Eph receptors. Bioactive
     ephrin mimetic peptides could be used to selectively deliver
     agents to Eph receptor-expressing tissues and modify
     Eph signaling in therapies for cancer, pathol. angiogenesis, and
     nerve regeneration.
ST
     ephrin mimetic peptide target EphA2 receptor
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin A2; ephrin mimetic peptide that selectively
        targets the EphA2 receptor tyrosine
       kinase and stimulates signaling)
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin A; ephrin mimetic peptide that selectively
        targets the EphA2 receptor tyrosine
       kinase and stimulates signaling)
IT
     Human
     Peptide library
     Signal transduction, biological
        (ephrin mimetic peptide that selectively targets the
        EphA2 receptor tyrosine kinase
        and stimulates signaling)
IT
     Peptides, biological studies
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (ephrin mimetic peptide that selectively targets the
        EphA2 receptor tyrosine kinase
        and stimulates signaling)
TΤ
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin mimetic peptide that selectively targets the
        EphA2 receptor tyrosine kinase
        and stimulates signaling)
IT
                                 532441-11-5
                                               532441-12-6
     532441-09-1 532441-10-4
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
```

(ephrin mimetic peptide that selectively targets the
BphA2 receptor tyrosine kinase
and stimulates signaling)

- RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD RE
- (1) Andres, A; Oncogene 1994, V9, P1461 HCAPLUS
- (2) Arap, W; Proc Natl Acad Sci U S A 2002, V99, P1527 HCAPLUS
- (3) Arap, W; Science 1998, V279, P377 HCAPLUS
- (4) Carles-Kinch, K; Cancer Res 2002, V62, P2840 HCAPLUS
- (5) Cheng, H; Cell 1994, V79, P157 HCAPLUS
- (6) Daniel, T; Kidney Int Suppl 1996, V57, PS73 HCAPLUS
- (7) Devlin, J; Science 1990, V249, P404 HCAPLUS
- (8) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS
- (9) Dohn, M; Oncogene 2001, V20, P6503 HCAPLUS
- (10) Dvorak, H; Am J Pathol 1988, V133, P95 MEDLINE
- (11) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
- (12) Ellerby, H; Nat Med 1999, V5, P1032 HCAPLUS
- (13) Eph Nomenclature Committee; Cell 1997, V90, P403
- (14) Essler, M; Proc Natl Acad Sci U S A 2002, V99, P2252 HCAPLUS
- (15) Flanagan, J; Annu Rev Neurosci 1998, V21, P309 HCAPLUS
- (16) Ganju, P; Oncogene 1994, V9, P1613 HCAPLUS
- (17) Gerlag, D; Arthritis Res 2001, V3, P357 HCAPLUS
- (18) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS
- (19) Himanen, J; Nature 1998, V396, P486 HCAPLUS
- (20) Himanen, J; Nature 2001, V414, P933 HCAPLUS
- (21) Hornberger, M; Neuron 1999, V22, P731 HCAPLUS
- (22) Koivunen, E; J Biol Chem 1993, V268, P20205 HCAPLUS
- (23) Koivunen, E; J Cell Biol 1994, V124, P373 HCAPLUS
- (24) Koivunen, E; Nat Biotechnol 1999, V17, P768 HCAPLUS
- (25) Labrador, J; EMBO J 1997, V16, P3889 HCAPLUS
- (26) McBride, J; Mech Dev 1998, V77, P201 HCAPLUS
- (27) Menzel, P; Dev Biol 2001, V230, P74 HCAPLUS
- (28) Miao, H; Nature Cell Biol 2001, V3, P527 HCAPLUS
- (29) Miranda, J; Exp Neurol 1999, V156, P218 HCAPLUS
- (30) Myers, C; J Cell Biol 2000, V148, P343 HCAPLUS
- (31) Nemoto, T; Pathobiology 1997, V65, P195 HCAPLUS
- (32) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
- (33) Olson, T; Int J Cancer 1997, V73, P865 HCAPLUS
- (34) Pandey, A; Science 1995, V268, P567 HCAPLUS
- (35) Pasqualini, R; J Cell Biol 1995, V130, P1189 HCAPLUS
- (36) Rajotte, D; J Biol Chem 1999, V274, P11593 HCAPLUS
- (37) Rodger, J; Eur J Neurosci 2001, V14, P1929 MEDLINE
- (38) Ruiz, J; Mech Dev 1994, V46, P87 HCAPLUS
- (39) Smith, G; Science 1985, V228, P1315 MEDLINE
- (40) van der Geer, P; Annu Rev Cell Biol 1994, V10, P251 HCAPLUS
- (41) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
- (42) Wang, B; Biochemistry 1999, V38, P12499 HCAPLUS
- (43) Wright, R; Bio-Technology 1995, V13, P165 HCAPLUS
- (44) Yancopoulos, G; Nature 2000, V407, P242 HCAPLUS
- (45) Yayon, A; Proc Natl Acad Sci U S A 1993, V90, P10643 HCAPLUS
- (46) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
- (47) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
- (48) Zelinski, D; J Cell Biochem 2002, V85, P714 HCAPLUS
- L40 ANSWER 29 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2002:822127 HCAPLUS
- DN 138:104526
- ED Entered STN: 29 Oct 2002
- TI Diverse roles for the Eph family receptor tyrosine kinases in carcinogenesis

```
ΑU
     Nakamoto, Masaru; Bergemann, Andrew D.
     Department of Neurosciences/NC30, Lerner Research Institute, The Cleveland
CS
     Clinic Foundation, Cleveland, OH, 44195, USA
     Microscopy Research and Technique (2002), 59(1), 58-67
SO
     CODEN: MRTEEO; ISSN: 1059-910X
PB
     Wiley-Liss, Inc.
DT
     Journal; General Review
LΑ
     English
CC
     14-0 (Mammalian Pathological Biochemistry)
AB
     A review. The Eph family of receptor Tyr
     kinases and their cell-presented ligands, the ephrins,
     are frequently overexpressed in a wide variety of cancers, including
     breast, small-cell lung and gastrointestinal cancers, melanomas, and
     neuroblastomas. In particular, one Eph family member,
     EphA2, is overexpressed in many cancers, including 40% of breast
     cancers. EphA2 can also transform breast epithelial cells in
     vitro to display properties commonly associated with the development of
     metastasis. Remarkably, the oncogenic properties of EphA2
     contravene traditional dogma with regard to the oncogenic properties of a
     growth factor and its receptor tyrosine kinase
     : while stimulation of EphA2 by its ligand (ephrin-A1)
     results in EphA2 autophosphorylation, the stimulation reverses
     the oncogenic transformation. As will be discussed in this review, the
     apparent dependence of oncogenicity on the dephosphorylated state of
     EphA2 most probably reflects the unique nature of Eph
     signaling. In particular, oncogenecity may depend on the capacity of
     unactivated EphA2 to interact with a variety of signaling mols.
     As well as acting in oncogenic transformation, a growing body of evidence
     supports the importance of the concerted actions of ephrins and
     Eph mols. in tumor angiogenesis. Genetic studies, using targeted
     mutagenesis in mice, reveal that ephrin-B1, ephrin-B2,
     and EphB4 are essential for the normal morphogenesis of the
     embryonic vasculature into a sophisticated network of arteries, veins, and
     capillaries. Initial studies indicate that these mols. are also
     angiogenic in tumors, and as such represent important new targets for the
     development of chemotherapeutic treatments.
ST
     review Eph receptor tyrosine kinase
     ephrin tumorigenesis
IT
     Transformation, neoplastic
        (Eph family receptor Tyr kinases in
        carcinogenesis)
TT
     Proteins
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); BIOL (Biological study)
        (ephrin; Eph family receptor Tyr
        kinases in carcinogenesis)
IT
     149433-92-1, Eph receptor tyrosine
     kinase
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); BIOL (Biological study)
        (Eph family receptor Tyr kinases in
        carcinogenesis)
              THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
       126
RE
(1) Adams, R; Cell 2001, V104, P57 HCAPLUS
(2) Adams, R; Genes Dev 1999, V13, P295 HCAPLUS
(3) Andres, A; Oncogene 1991, V6, P771 HCAPLUS
(4) Andres, A; Oncogene 1994, V9, P1461 HCAPLUS
(5) Bartley, T; Nature 1994, V368, P558 HCAPLUS
(6) Becker, N; Mech Dev 1994, V47, P3 HCAPLUS
```

- (7) Beckmann, M; EMBO J 1994, V13, P3757 HCAPLUS (8) Bennett, B; J Biol Chem 1994, V269, P14211 HCAPLUS (9) Berclaz, G; Biochem Biophys Res Commun 1996, V226, P869 HCAPLUS (10) Bergemann, A; Mol Cell Biol 1995, V15, P4921 HCAPLUS (11) Birgbauer, E; Development 2000, V127, P1231 HCAPLUS (12) Bohme, B; Oncogene 1993, V8, P2857 MEDLINE (13) Bovenkamp, D; DNA Cell Biol 2001, V20, P203 HCAPLUS (14) Boyd, A; J Biol Chem 1992, V267, P3262 HCAPLUS (15) Brambilla, R; EMBO J 1995, V14, P3116 HCAPLUS (16) Bruce, V; Brain Res 1999, V821, P169 HCAPLUS (17) Bruckner, K; Neuron 1999, V22, P511 HCAPLUS (18) Bruckner, K; Science 1997, V275, P1640 MEDLINE (19) Buchert, M; J Cell Biol 1999, V144, P361 HCAPLUS (20) Cantley, L; Cell 1991, V64, P281 HCAPLUS (21) Chaib, H; Neoplasia 2001, V3, P43 HCAPLUS (22) Chen, W; Int J Cancer 1999, V83, P579 HCAPLUS (23) Cheng, H; Cell 1995, V82, P371 HCAPLUS (24) Chiari, R; Cancer Res 2000, V60, P4855 HCAPLUS (25) Clark, G; Oncogene 1996, V12, P169 HCAPLUS (26) Davis, S; Science 1994, V266, P816 HCAPLUS (27) Davy, A; EMBO J 2000, V19, P5396 HCAPLUS (28) Davy, A; Genes Dev 1999, V13, P3125 HCAPLUS (29) Dodelet, V; J Biol Chem 1999, V274, P31941 HCAPLUS (30) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS (31) Dottori, M; Blood 1999, V94, P2477 HCAPLUS (32) Drescher, U; Cell 1995, V82, P359 HCAPLUS (33) Easty, D; Cancer Res 1995, V55, P2528 HCAPLUS (34) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS (35) Easty, D; Int J Cancer 1997, V71, P1061 HCAPLUS (36) Easty, D; Int J Cancer 1999, V84, P494 HCAPLUS (37) Easty, D; Melanoma Res 2000, V10, P401 HCAPLUS (38) Ellis, C; Oncogene 1996, V12, P1727 HCAPLUS (39) Eph Nomenclature Committee; Cell 1997, V90, P403 (40) Even-Ram, S; J Biol Chem 2001, V276, P10952 HCAPLUS (41) Flanagan, J; Annu Rev Neurosci 1998, V21, P309 HCAPLUS (42) Frisch, S; J Cell Biol 1996, V134, P793 HCAPLUS (43) Gale, N; Dev Biol 2001, V230, P151 HCAPLUS (44) Gale, N; Neuron 1996, V17, P9 HCAPLUS (45) George, S; Cell 1998, V92, P633 HCAPLUS (46) Gerety, S; Mol Cell 1999, V4, P403 HCAPLUS (47) Giunciuglio, D; Int J Cancer 1995, V63, P815 HCAPLUS (48) Gu, C; Mol Cell Biol 2001, V21, P4579 HCAPLUS (49) Helbling, P; Development 2000, V127, P269 HCAPLUS (50) Henkemeyer, M; Cell 1996, V86, P35 HCAPLUS (51) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS (52) Himanen, J; Nature 1998, V396, P486 HCAPLUS (53) Hirai, H; Science 1987, V238, P1717 HCAPLUS (54) Hock, B; Oncogene 1998, V17, P255 HCAPLUS (55) Holland, S; EMBO J 1997, V16, P3877 HCAPLUS (56) Holland, S; Nature 1996, V383, P722 HCAPLUS (57) Holmberg, J; Nature 2000, V408, P203 HCAPLUS (58) Huai, J; J Biol Chem 2001, V276, P6689 HCAPLUS (59) Ikegaki, N; Hum Mol Genet 1995, V4, P2033 HCAPLUS (60) Ilangumaran, S; Immunol Today 2000, V21, P2 HCAPLUS (61) Iwase, T; Biochem Biophys Res Commun 1993, V194, P698 HCAPLUS
 - jan delaval 7 july 2005

(62) Kalo, M; Biochemistry 1999, V38, P14396 HCAPLUS
(63) Kinch, M; J Cell Biol 1995, V130, P461 HCAPLUS
(64) Kiyokawa, E; Cancer Res 1994, V54, P3645 HCAPLUS
(65) Knoll, B; Development 2001, V128, P895 HCAPLUS
(66) Kozlosky, C; Oncogene 1995, V10, P299 HCAPLUS

- (67) Krull, C; Curr Biol 1997, V7, P571 HCAPLUS
- (68) Kumar, R; Semin Oncol 2000, V27, P84 HCAPLUS
- (69) Lackmann, M; J Biol Chem 1998, V273, P20228 HCAPLUS
- (70) Lamorte, L; Surg Oncol Clin N Am 2001, V10, P271 MEDLINE
- (71) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
- (72) Lu, Q; Cell 2001, V105, P69 HCAPLUS
- (73) Maru, Y; Mol Cell Biol 1988, V8, P3770 HCAPLUS
- (74) Maru, Y; Oncogene 1990, V5, P445 HCAPLUS
- (75) McBride, J; Mech Dev 1998, V77, P201 HCAPLUS
- (76) Mellitzer, G; Nature 1999, V400, P77 HCAPLUS
- (77) Menzel, P; Dev Biol 2001, V230, P74 HCAPLUS
- (78) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
- (79) Miao, H; Nat Cell Biol 2001, V3, P527 HCAPLUS
- (80) Miescher, G; Brain Res Mol Brain Res 1997, V46, P17 HCAPLUS
- (81) Munthe, E; FEBS Lett 2000, V466, P169 HCAPLUS
- (82) Nakamoto, M; Cell 1996, V86, P755 HCAPLUS
- (83) Nieto, M; Development 1992, V116, P1137 HCAPLUS
- (84) Nikolova, Z; J Cell Sci 1998, V111, P2741 HCAPLUS
- (85) Oba, S; Cancer Lett 2001, V164, P97 HCAPLUS
- (86) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
- (87) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS
- (88) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS
- (89) Robinson, D; Proc Natl Acad Sci 1996, V93, P5958 HCAPLUS
- (90) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
- (91) Ruoslahti, E; Princess Takamatsu Symp 1994, V24, P99 MEDLINE
- (92) Saarma, M; Eur J Biochem 2000, V267, P6968 HCAPLUS
- (93) Sakano, S; Oncogene 1996, V13, P813 HCAPLUS
- (94) Schoenenberger, C; EMBO J 1988, V7, P169 HCAPLUS
- (95) Segatto, O; Mol Cell Biol 1988, V8, P5570 HCAPLUS
- (96) Shamah, S; Cell 2001, V105, P233 HCAPLUS
- (97) Shen, Y; Mol Biol Cell 1999, V10, P2507 HCAPLUS
- (98) Shimoyama, M; Growth Factors 2000, V18, P63 MEDLINE
- (99) Shin, D; Dev Biol 2001, V230, P139 HCAPLUS
- (100) Simons, K; Nature 1997, V387, P569 HCAPLUS
- (101) Smalla, M; Protein Sci 1999, V8, P1954 HCAPLUS
- (102) Sommers, C; Breast Cancer Res Treat 1994, V31, P325 MEDLINE
- (103) Stein; E; Genes Dev 1998, V12, P667 HCAPLUS
- (104) Stein, E; J Biol Chem 1996, V271, P23588 HCAPLUS
- (105) Stein, E; J Biol Chem 1998, V273, P1303 HCAPLUS
- (106) Steube, K; Leuk Lymphoma 1999, V33, P371 HCAPLUS
- (107) Takai, N; Oncol Rep 2001, V8, P567 HCAPLUS
- (108) Tang, X; Clin Cancer Res 1999, V5, P455 HCAPLUS
- (109) Tang, X; Med Pediatr Oncol 2000, V35, P656 MEDLINE
- (110) Tang, X; Oncogene 1998, V17, P521 HCAPLUS
- (111) Tang, X; Proc Natl Acad Sci 2000, V97, P10936 HCAPLUS
- (112) Tessier-Lavigne, M; Cell 1995, V82, P345 HCAPLUS
- (113) Torres, R; Neuron 1998, V21, P1453 HCAPLUS
- (114) Tuzi, N; Br J Cancer 1994, V69, P417 HCAPLUS
- (115) Vogt, T; Clin Cancer Res 1998, V4, P791 HCAPLUS
- (116) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
- (117) Wang, H; Cell 1998, V93, P741 HCAPLUS
- (118) Wang, H; Neuron 1997, V18, P383 HCAPLUS
- (119) Weaver, V; Semin Cancer Biol 1995, V6, P175 HCAPLUS
- (120) Wicks, I; Proc Natl Acad Sci 1992, V89, P1611 HCAPLUS
- (121) Winslow, J; Neuron 1995, V14, P973 HCAPLUS
- (122) Xu, L; J Biol Chem 2000, V275, P30597 HCAPLUS
- (123) Xu, Q; Development 1995, V121, P4005 HCAPLUS
- (124) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
- (125) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
- (126) Zisch, A; Oncogene 1998, V16, P2657 HCAPLUS

```
L40 ANSWER 30 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
     2002:811847 HCAPLUS
AN
DN
     138:301095
ED
     Entered STN: 25 Oct 2002
TI
     Activation of the EphA2 tyrosine kinase
     stimulates the MAP/ERK kinase signaling cascade
ΑU
     Pratt, Rebecca L.; Kinch, Michael S.
     Department of Basic Medical Sciences, Purdue University Cancer Center,
CS
     West Lafayette, IN, 47907-1246, USA
so
     Oncogene (2002), 21(50), 7690-7699
     CODEN: ONCNES; ISSN: 0950-9232
PB
     Nature Publishing Group
     Journal
DT
LA
     English
CC
     13-6 (Mammalian Biochemistry)
AB
     Intracellular signaling by receptor tyrosine
     kinases regulates many different aspects of cell behavior.
     studies in our laboratory and others have demonstrated that the EphA2
     receptor tyrosine kinase critically regulates
     tumor cell growth, migration and invasiveness. Although the cellular
     consequences of EphA2 signaling have been the focus of recent
     attention, the biochem. changes that are triggered by ligand-mediated
     activation of EphA2 remain largely unknown. Herein, we
     demonstrate that ligand stimulation of EphA2 promotes the
     nucleus translocation and phosphorylation of ERK kinases,
     followed by an increase in nuclear induction of the Elk-1 transcription
     factor. Ligand-mediated activation allows EphA2 to form a mol.
     complex with the SHC and GRB2 adaptor proteins. Specifically,
     we demonstrate that tyrosine phosphorylated EphA2
     interacts with the PTB and SH2 domains of SHC. We also show that the
     interaction of EphA2 with GRB2 is indirect and mediated by SHC
     and that this complex is necessary for EphA2-mediated activation
     of ERK kinases. These studies provide a novel mechanism to
     demonstrate how EphA2 can convey information from the cell
     exterior to the nucleus.
     EphA2 kinase activation MAP ERK kinase
ST
     signal transduction
IT
     Transcription factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ELK-1; activation of the EphA2 tyrosine
        kinase stimulation of MAP/ERK kinase signaling
        cascade in relation to)
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (GRB-2 (growth factor receptor-bound protein 2);
        SHC activation of GRB2 and EphA2 tyrosine
        kinase stimulation of MAP/ERK kinase signaling
        cascade)
TT
    Molecular association
        (SHC activation of GRB2 and EphA2 tyrosine
        kinase stimulation of MAP/ERK kinase signaling
        cascade)
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (SHC; SHC activation of the EphA2 tyrosine
        kinase stimulation of MAP/ERK kinase signaling
        cascade)
TT
     Signal transduction, biological
        (activation of the EphA2 tyrosine kinase
```

stimulation of MAP/ERK kinase signaling cascade) IT Cell nucleus (activation of the EphA2 tyrosine kinase stimulation of MAP/ERK kinase signaling cascade and nucleus translocation) IT Biological transport (intracellular; activation of the EphA2 tyrosine kinase stimulation of MAP/ERK kinase signaling cascade and nucleus translocation) IT Phosphorylation, biological (protein; activation of the EphA2 tyrosine kinase stimulation of MAP/ERK kinase signaling cascade in relation to) 142243-02-5, ERK kinase 149433-91-0, EphA2 IT receptor tyrosine kinase RL: BSU (Biological study, unclassified); BIOL (Biological study) (activation of the EphA2 tyrosine kinase stimulation of MAP/ERK kinase signaling cascade) THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD RE (1) Aliaga, J; Am J Physiol 1999, V277, PG631 HCAPLUS (2) Bartley, T; Nature 1994, V368, P558 HCAPLUS (3) Blumer, K; Trends Biochem Sci 1994, V19, P236 HCAPLUS (4) Borg, J; Curr Top Microbiol Immunol 1998, V228, P23 HCAPLUS (5) Brennan, C; Development 1997, V124, P655 HCAPLUS (6) Brunet, A; Comptes Rendus des Seances de la Societe de Biologie et de Ses Filiales 1995, V189, P43 HCAPLUS (7) Carpenter, M; J Neurosci Res 1995, V42, P199 HCAPLUS (8) Cattaneo, E; Trends Neurosci 1998, V21, P476 HCAPLUS (9) Charest, A; J Biol Chem 1996, V271, P8424 HCAPLUS (10) Clarkson, R; Mol Endocrinol 1999, V13, P619 HCAPLUS (11) Cowley, S; Cell 1994, V77, P841 HCAPLUS (12) Davis, R; Mol Repro Dev 1995, V42, P459 HCAPLUS (13) Davis, S; Science 1994, V266, P816 HCAPLUS (14) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS (15) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS (16) Elowe, S; Mol Cell Biol 2001, V21, P7429 HCAPLUS (17) Gonzalez, F; J Cell Biol 1993, V122, P1089 HCAPLUS (18) Graham, F; Virology 1973, V52, P456 MEDLINE (19) Graham, S; Mol Cell Biol 1996, V16, P6132 HCAPLUS (20) Hunter, T; Philos Trans R Soc Lond B Biol Sci 1998, V353, P583 HCAPLUS (21) Lenormand, P; J Cell Biol 1998, V142, P625 HCAPLUS (22) Lin, T; J Cell Biol 1997, V136, P1385 HCAPLUS (23) Lu, Q; Biol Repro 2002, V66, P29 HCAPLUS (24) Luzi, L; Curr Opin Genet Dev 2000, V10, P668 HCAPLUS (25) Macleod, K; Trends Biochem Sci 1992, V17, P251 HCAPLUS (26) McCormick, B; Pharmacol Ther 1992, V53, P239 MEDLINE (27) McNeil, P; Fluorescence Microscopy of Living Cells in Culture 1989, P153 **HCAPLUS** (28) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS (29) Miao, H; Nat Cell Biol 2001, V3, P527 HCAPLUS (30) Morris, M; Curr Opin Biotechnol 2000, V11, P461 HCAPLUS (31) Morris, M; J Biol Chem 2000, V275, P28849 HCAPLUS (32) Nakamoto, M; Cell 1996, V86, P755 HCAPLUS (33) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS (34) Pandey, A; Science 1995, V268, P567 HCAPLUS

- (36) Pawson, T; Nature 1995, V373, P573 HCAPLUS
 (37) Pawson, T; Science 1998, V278, P2075
- (38) Reese, D; Stem Cells 1997, V15, P1 HCAPLUS

jan delaval - 7 july 2005

(35) Pasquale, E; Curr Opin Cell Biol 1997, V9, P608 HCAPLUS

- haddad 10 / 823259 (39) Roovers, K; Bioessays 2000, V22, P818 HCAPLUS (40) Roovers, K; Mol Biol Cell 1999, V10, P3197 HCAPLUS (41) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS (42) Scheid, M; Curr Biol 2000, V10, PR191 HCAPLUS (43) Schramek, H; J Biol Chem 1997, V272, P11426 HCAPLUS (44) Shao, H; J Biol Chem 1995, V270, P5636 HCAPLUS (45) Stein, E; Genes Dev 1998, V12, P667 HCAPLUS (46) Townsend, K; J Biol Chem 1999, V274, P1801 HCAPLUS (47) Treisman, R; Curr Opin Genet Dev 1994, V4, P96 HCAPLUS (48) van der Geer, P; Trends Biochem Sci 1995, V20, P277 HCAPLUS (49) Vanhoutte, P; J Biol Chem 2001, V276, P5189 HCAPLUS (50) Verlhac, M; EMBO J 2000, V19, P6065 HCAPLUS (51) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS (52) Wang, H; Neuron 1997, V18, P383 HCAPLUS (53) Yarden, Y; Nat Rev Mol Cell Biol 2001, V2, P127 HCAPLUS (54) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS (55) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS (56) Zohn, I; Mol Cell Biol 1998, V18, P1225 HCAPLUS L40 ANSWER 31 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN AN 2002:783137 HCAPLUS DN 138:53504 ED Entered STN: 15 Oct 2002 ΤI Regulation of the EphA2 kinase by the low molecular weight tyrosine phosphatase induces transformation ΑU Kikawa, Keith D.; Vidale, Derika R.; Van Etten, Robert L.; Kinch, Michael S. CS Department of Basic Medical Sciences, Purdue University, West Lafayette, IN, 47907, USA SO Journal of Biological Chemistry (2002), 277(42), 39274-39279 CODEN: JBCHA3; ISSN: 0021-9258 PB American Society for Biochemistry and Molecular Biology DTJournal LA English CC 14-1 (Mammalian Pathological Biochemistry) AB Intracellular signaling by protein tyrosine phosphorylation is generally understood to govern many aspects of cellular behavior. The biol. consequences of this signaling pathway are important because the levels of protein tyrosine phosphorylation are frequently elevated in cancer cells. In the classic paradigm, tyrosine kinases promote tumor cell growth, survival, and invasiveness, whereas tyrosine phosphatases neg. regulate these same behaviors. Here, we identify one particular tyrosine phosphatase, low mol. weight tyrosine phosphatase (LMW-PTP), which is frequently overexpressed in transformed cells. We also show that overexpression of LMW-PTP is sufficient to confer transformation upon non-transformed epithelial cells. Notably, we show that the EphA2 receptor tyrosine kinase is a prominent substrate for LMW-PTP and that the oncogenic activities of LMW-PTP result from altered EphA2 expression and function. These results suggest a role for LMW-PTP in transformation progression and link its oncogenic potential to EphA2. ST EphA2 LMW tyrosine phosphatase signaling assocn neoplastic transformation
- IT Molecular association

(EphA2 and LMW-PTP form mol. complex in vivo)

IT Phosphorylation, biological

(protein, of protein tyrosine; regulation of EphA2 kinase by low mol. weight tyrosine phosphatase induces transformation)

```
IT
     Dephosphorylation, biological
     Human
     Neoplasm
     Signal transduction, biological
     Transformation, neoplastic
        (regulation of EphA2 kinase by low mol. weight
        tyrosine phosphatase induces transformation)
     60-18-4, L-Tyrosine, biological studies
IT
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); PRP (Properties); BIOL (Biological study)
        (phosphorylation; regulation of EphA2 kinase by low
        mol. weight tyrosine phosphatase induces transformation)
IT
     149433-91-0, EphA2 receptor tyrosine
            352548-19-7, Phosphatase, protein
    phosphotyrosine, LMW
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); BIOL (Biological study)
        (regulation of EphA2 kinase by low mol. weight
        tyrosine phosphatase induces transformation)
              THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RE
(1) Andres, A; Int J Cancer 1995, V63, P288 HCAPLUS
(2) Birchmeier, W; Bioessays 1995, V17, P97 HCAPLUS
(3) Bryson, G; Genomics 1995, V30, P133 HCAPLUS
(4) Carles-Kinch, K; Cancer Res 2001, V62, P2840
(5) Cates, C; Cancer Lett 1996, V110, P49 HCAPLUS
(6) Clark, G; Oncogene 1996, V12, P169 HCAPLUS
(7) Cobb, B; Oncogene 1993, V8, P2897 HCAPLUS
(8) Easty, D; Cancer Res 1995, V55, P2528 HCAPLUS
(9) Fiaschi, T; J Biol Chem 2001, V276, P49156 HCAPLUS
(10) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS
(11) Hunter, T; Cell 2000, V100, P113 HCAPLUS
(12) Jacob, A; Cancer Detect Prev 1999, V23, P325 HCAPLUS
(13) Kinch, M; J Cell Biol 1995, V130, P461 HCAPLUS
(14) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
(15) Liu, X; Recent Prog Horm Res 1994, V49, P149 HCAPLUS
(16) Miao, H; Nat Cell Bio 2000, V2, P62 HCAPLUS
(17) Paine, T; Int J Cancer 1992, V50, P463 MEDLINE
(18) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS
(19) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS
(20) Pawson, T; Science 1997, V278, P2075 HCAPLUS
(21) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
(22) Shevrin, D; Prostate 1989, V15, P187 MEDLINE
(23) Shimizu, H; Biochem Biophys Res Commun 2001, V289, P602 HCAPLUS
(24) Stein, E; Genes Dev 1998, V12, P667 HCAPLUS
(25) Sun, X; Cell Growth & Differ 1999, V10, P343 HCAPLUS
(26) Volberg, T; Cell Regul 1991, V2, P105 HCAPLUS
(27) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
(28) Wo, Y; Biochemistry 1992, V31, P1712 HCAPLUS
(29) Zantek, N; Cell Growth & Differ 1999, V10, P629 HCAPLUS
(30) Zantek, N; Clin Cancer Res 2001, V7, P3640 HCAPLUS
(31) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
(32) Zhang, M; J Biol Chem 1998, V273, P21714 HCAPLUS
(33) Zhang, Z; J Biol Chem 1994, V269, P25947 HCAPLUS
L40
    ANSWER 32 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2002:758670 HCAPLUS
DN
     138:22838
ED
     Entered STN: 07 Oct 2002
     Soluble Eph A receptors inhibit
ΤI
```

```
tumor angiogenesis and progression in vivo
ΙIΑ
     Brantley, Dana M.; Cheng, Nikki; Thompson, Erin J.; Lin, Qing; Brekken,
     Rolf A.; Thorpe, Philip E.; Muraoka, Rebecca S.; Cerretti, Douglas Pat;
     Pozzi, Ambra; Jackson, Dowdy; Lin, Charles; Chen, Jin
CS
    Department of Medicine, Vanderbilt University School of Medicine,
    Nashville, TN, 37232, USA
SO
     Oncogene (2002), 21(46), 7011-7026
     CODEN: ONCNES; ISSN: 0950-9232
PB
    Nature Publishing Group
    Journal
DT
LΑ
     English
CC
     14-1 (Mammalian Pathological Biochemistry)
AB
     The Eph family of receptor tyrosine
     kinases and their ligands, known as ephrins, play a
     crucial role in vascular development during embryogenesis. The function
     of these mols. in adult angiogenesis has not been well characterized.
    Here, we report that blocking Eph A class
     receptor activation inhibits angiogenesis in two
     independent tumor types, the RIP-Tag transgenic model of
     angiogenesis-dependent pancreatic islet cell carcinoma and the 4T1 model
     of metastatic mammary adenocarcinoma. Ephrin-Al ligand was
     expressed in both tumor and endothelial cells, and EphA2
     receptor was localized primarily in tumor-associated vascular
     endothelial cells. Soluble EphA2-Fc or EphA3-Fc
     receptors inhibited tumor angiogenesis in cutaneous
     window assays, and tumor growth in vivo. EphA2-Fc or
     EphA3-Fc treatment resulted in decreased tumor vascular d., tumor
     volume, and cell proliferation, but increased cell apoptosis. However,
     EphA2-Fc had no direct effect on tumor cell growth or apoptosis in
     culture, yet inhibited migration of endothelial cells in
     response to tumor cells, suggesting that the soluble receptor
     inhibited blood vessel recruitment by the tumor. These data
    provide the first functional evidence for Eph A class
     receptor regulation of pathogenic angiogenesis induced by tumors
     and support the function of A class Eph receptors in
     tumor progression.
ST
     ephrin A receptor tumor angiogenesis
ΙT
     Mammary gland, neoplasm
        (adenocarcinoma, metastasis; soluble Eph A
        receptors inhibit tumor angiogenesis and progression
        in vivo)
IT
     Pancreatic islet of Langerhans, neoplasm
        (carcinoma; soluble Eph A receptors
        inhibit tumor angiogenesis and progression in vivo)
IT
    Blood vessel
        (endothelium; soluble Eph A receptors
        inhibit tumor angiogenesis and progression in vivo)
IT
    Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin-A1; soluble Eph A receptors
        inhibit tumor angiogenesis and progression in vivo)
IT
    Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin-A2, soluble complexes, with Fc; soluble Eph
        A receptors inhibit tumor angiogenesis and
        progression in vivo)
IT
    Receptors
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin-A2; soluble Eph A receptors
        inhibit tumor angiogenesis and progression in vivo)
```

```
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin-A3, soluble complexes, with Fc; soluble Eph
        A receptors inhibit tumor angiogenesis and
        progression in vivo)
IT
     Carcinoma
        (mammary adenocarcinoma, metastasis; soluble Eph A
        receptors inhibit tumor angiogenesis and progression
        in vivo)
TΤ
     Carcinoma
        (pancreatic islet; soluble Eph A receptors
        inhibit tumor angiogenesis and progression in vivo)
IT
     Angiogenesis
    Human
        (soluble Eph A receptors inhibit
        tumor angiogenesis and progression in vivo)
IT
     Endothelium
        (vascular; soluble Eph A receptors
        inhibit tumor angiogenesis and progression in vivo)
RE.CNT
              THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Aaltomaa, S; J Cancer Res Clin Oncol 1993, V119, P288 MEDLINE
(2) Adams, R; Genes Dev 1999, V3, P295
(3) Adams, R; Genes Dev 1999, V13, P295 HCAPLUS
(4) Arbiser, J; Proc Natl Acad Sci USA 1997, V94, P861 HCAPLUS
(5) Aslakson, C; Cancer Res 1992, V52, P1399 MEDLINE
(6) Bergers, G; Nat Cell Biol 2000, V2, P737 HCAPLUS
(7) Bergers, G; Science 1999, V284, P808 HCAPLUS
(8) Brantley, D; Mech Dev 2000, V97, P149 HCAPLUS
(9) Brantley, D; Mol Biol Cell 2001, V12, P1445 HCAPLUS
(10) Brekken, R; Cancer Res 1998, V58, P1952 HCAPLUS
(11) Chen, J; J Biol Chem 1998, V273, P24670 HCAPLUS
(12) Cheng, N; Cytokine and Growth Factor Reviews 2002, V13, P75 HCAPLUS
(13) Daniel, T; Kidney Int Suppl 1996, V57, PS73 HCAPLUS
(14) Dankort, D; Transgenic models of breast cancer metastasis 1996
(15) Davis, S; Science 1994, V266, P816 HCAPLUS
(16) Davy, A; EMBO J 2000, V19, P5396 HCAPLUS
(17) Davy, A; Genes Dev 1999, V13, P3125 HCAPLUS
(18) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
(19) Easty, D; Int J Cancer 1999, V84, P494 HCAPLUS
(20) Folkman, J; J Clin Oncol 1994, V12, P441 MEDLINE
(21) Folkman, J; J Natl Cancer Inst 1990, V82, P4 MEDLINE
(22) Folkman, J; Nature 1989, V339, P58 MEDLINE
(23) Gale, N; Cell Tissue Res 1997, V290, P227 HCAPLUS
(24) Gale, N; Genes Dev 1999, V13, P1055 HCAPLUS
(25) Gerety, S; Molecular Cell 1999, V4, P403 HCAPLUS
(26) Goede, V; Anticancer Res 1998, V18, P2199 MEDLINE
(27) Hanahan, D; Nature 1985, V315, P115 HCAPLUS
(28) Hattori, M; Science 2000, V289, P1360 HCAPLUS
(29) Holder, N; Development 1999, V126, P2033 HCAPLUS
(30) Holzman, L; Mol Cell Biol 1990, V10, P5830 HCAPLUS
(31) Huai, J; J Biol Chem 2001, V276, P6689 HCAPLUS
(32) Huang, Q; Nat Biotechnol 1999, V17, P1033 HCAPLUS
(33) Kuehn, R; Pancreas 1999, V18, P96 MEDLINE
(34) Laferriere, J; J Biol Chem 2001, V276, P33762 HCAPLUS
(35) Li, C; J Natl Cancer Inst 2000, V92, P143 MEDLINE
(36) Lin, P; Proc Natl Acad Sci USA 1998, V95, P8829 HCAPLUS
(37) McBride, J; Nech Dev 1998, V77, P201 HCAPLUS
(38) Muraoka, R; J Cell Biol 2001, V153, P917 HCAPLUS
(39) Myers, C; J Cell Biol 2000, V148, P343 HCAPLUS
```

- (40) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
- (41) Owens, R; J Natl Cancer Inst 1974, V53, P261 MEDLINE
- (42) Pandey, A; Science 1995, V268, P567 HCAPLUS
- (43) Papenfuss, H; Microvasc Res 1979, V18, P311 MEDLINE
- (44) Passaniti, A; Lab Invest 1992, V67, P519 MEDLINE
- (45) Prewett, M; Cancer Res 1999, V59, P5209 HCAPLUS
- (46) Preziosi, R; J Comp Pathol 1995, V113, P301 HCAPLUS
- (47) Radvanyi, F; Mol Cell Biol 1993, V13, P4223 HCAPLUS
- (48) Rockwell, S; Br J Cancer Suppl 1978, V37, P212 HCAPLUS
- (49) Rockwell, S; Cancer Res 1981, V41, P527 MEDLINE
- (50) Rockwell, S; Int J Radiat Biol Relat Stud Phys Chem Med 1977, V31, P153 MEDLINE
- (51) Van den Broecke, C; Clin Exp Metastasis 1996, V14, P282 MEDLINE
- (52) Walker-Daniels, J; The Prostate 1999, V41, P275 HCAPLUS
- (53) Wang, H; Cell 1998, V93, P741 HCAPLUS
- (54) Weidner, N; Angiogenesis and breast cancer 1996
- (55) Weidner, N; J Natl Cancer Inst 1992, V84, P1875 MEDLINE
- (56) Weidner, N; N Engl J Med 1991, V324, P1 MEDLINE
- (57) Yancopoulos, G; Nature 2000, V407, P242 HCAPLUS
- (58) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
- (59) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
- L40 ANSWER 33 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2002:618525 HCAPLUS
- ED Entered STN: 16 Aug 2002
- TI Design and synthesis of **tyrosine** phosphatase inhibitor directed toward new cancer treatments
- AU Zabell, Adam P. R.; Stauffacher, Cynthia; Kinch, Michael; Katsuyama, Isamu; Wiest, Olaf; Helquist, Paul
- CS Walther Cancer Institute, Purdue University, West Lafayette, IN, 47907, USA
- SO Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), ORGN-130 Publisher: American Chemical Society, Washington, D. C. CODEN: 69CZPZ
- DT Conference; Meeting Abstract
- LA English
- One of the most important aspects in the treatment of cancer is the control of metastasis. We have been working on identification of tyrosine kinases and phosphatases, which are relevant to metastatic cancers. Recent studies have shown that unphosphorylated EphA2 tyrosine kinase participates in metastatic cell growth and invasiveness, that tyrosine phosphatase HCPTP is overexpressed in metastatic cells, and that HCPTP can dephosphorylate EphA2. Thus, designing inhibitors selective for HCPTP are expected to provide a novel mechanism to reduce or eliminate the metastatic effects of EphA2. On the basis of this concept, possible inhibitors have been proposed by use of computational design and their synthetic studies have subsequently been started. The recent progress on this work directed toward new cancer treatments will be reported.
- L40 ANSWER 34 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2002:580110 HCAPLUS
- DN 137:382619
- ED Entered STN: 05 Aug 2002
- TI Negative regulation of EphA2 receptor by Cbl
- AU Wang, You-jie; Ota, Satoshi; Kataoka, Hideki; Kanamori, Masao; Li, Zhong-you; Band, Hamid; Tanaka, Masamitsu; Sugimura, Haruhiko
- CS First Department of Pathology, Hamamatsu University School of Medicine,

```
Handayama, Hamamatsu, 431-3192, Japan
so
     Biochemical and Biophysical Research Communications (2002),
     296(1), 214-220
     CODEN: BBRCA9; ISSN: 0006-291X
PB
     Elsevier Science
DT
     Journal
LΑ
     English
     13-2 (Mammalian Biochemistry)
CC
AB
     The c-Cbl proto-oncogene product Cbl has emerged as a neg. regulator of
     receptor and non-receptor tyrosine
     kinases, a function dependent on its recently identified ubiquitin
     ligase activity. Here, we report that EphA2, a member of
     Eph receptor tyrosine kinases is
     neg. regulated by Cbl. The neg. regulation of EphA2 mediated by
     Cbl is dependent on the activity of EphA2, as the kinase
     inactive mutant of EphA2 cannot be regulated by Cbl. Moreover,
     a point mutation (G306E-Cbl) in TKB region of Cbl that has been reported
     to abolish Cbl binding to RTKs and non-receptor tyrosine
     kinases impaired the binding to active EphA2. The
     dominant neg. mutant 70Z-Cbl, which has a 17-amino acids deletion in the
     N-boundary of the RING finger domain, showed defunct neg. regulatory
     function of Cbl to EphA2. These results demonstrate that the
     TKB domain and RING finger domain of Cbl are essential for this neg.
     regulation.
ST
     Cbl protein EphA2 receptor tyrosine
     kinase
IT
     Protein motifs
        (RING finger; RING finger domain of Cbl in neg. regulation of
        EphA2 receptor)
IT
     Protein motifs
        (TKB (tyrosine kinase-binding) domain; TKB domain
        of Cbl in neg. regulation of EphA2 receptor)
IT
     Gene, animal
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (c-cbl; neg. regulation of EphA2 receptor by Cbl in
        relation to)
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (gene c-Cbl; neg. regulation of EphA2 receptor by
ΙT
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (neg. regulation of EphA2 receptor by Cbl)
              THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RE
(1) Bartkiewicz, M; J Biol Chem 1999, V274, P30887 HCAPLUS
(2) Blake, T; EMBO J 1993, V12, P2017 HCAPLUS
(3) Davis, S; Science 1994, V266, P816 HCAPLUS
(4) Dodelet, V; Oncogene 2000, V19, P5614 HCAPLUS
(5) Eph Nomenclature Committee; Cell 1997, V90, P403
(6) Holder, N; Development 1999, V126, P2033 HCAPLUS
(7) Holland, S; Nature 1996, V383, P722 HCAPLUS
(8) Huang, J; Mol Immunol 2000, V37, P1057 HCAPLUS
(9) Kiyokawa, E; Cancer Res 1994, V54, P3645 HCAPLUS
(10) Klein, R; Curr Opin Cell Biol 2001, V13, P196 HCAPLUS
(11) Levkowitz, G; Oncogene 1996, V12, P1117 HCAPLUS
(12) Lupher, M; Immunol Today 1999, V20, P375 HCAPLUS
(13) Meng, W; Nature 1999, V398, P84 HCAPLUS
(14) Miyake, S; J Biol Chem 1999, V274, P16619 HCAPLUS
```

```
(15) Miyake, S; Proc Natl Acad Sci USA 1998, V95, P7927 HCAPLUS
(16) Ota, S; J Biol Chem 2000, V275, P414 HCAPLUS
(17) Ota, Y; Science 1997, V276, P418 HCAPLUS
(18) Patan, S; J Neurooncol 2000, V50, P1 MEDLINE
(19) Tanaka, M; Mol Cell Biol 1995, V15, P6829 HCAPLUS
(20) Tanaka, M; Oncogene 1998, V17, P1509 HCAPLUS
(21) Tang, X; Clin Cancer Res 1999, V5, P455 HCAPLUS
(22) Yokouchi, M; J Biol Chem 1999, V274, P31707 HCAPLUS
    ANSWER 35 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
     2002:567861 HCAPLUS
AN
DN
     137:367053
     Entered STN: 31 Jul 2002
ED
     EphrinA1-induced cytoskeletal re-organization requires FAK and
AU
     Carter, Nigel; Nakamoto, Tetsuya; Hirai, Hisamaru; Hunter, Tony
     Molecular and Cell Biology Laboratory, The Salk Institute for Biological
CS
     Studies, La Jolla, CA, 92037, USA
SO
     Nature Cell Biology (2002), 4(8), 565-573
     CODEN: NCBIFN; ISSN: 1465-7392
PΒ
    Nature Publishing Group
DT
     Journal
LA
     English
CC
     13-6 (Mammalian Biochemistry)
AB
     Ephrins and Eph receptors are involved in
     axon guidance and cellular morphogenesis.
                                               An interaction between
     ephrin and Eph receptors elicits neuronal
     growth-cone collapse through cytoskeletal disassembly. When NIH3T3 cells
     were plated onto an ephrinAl-coated surface, the cells both
     adhered and spread. Adhesion and spreading proceeded concomitantly with
     changes in both the actin and microtubule cytoskeleton. EphA2,
     focal adhesion kinase (FAK) and pl30cas were identified as the
     major ephrin-dependent phosphotyrosyl proteins during
     the ephrin-induced morphol. changes. Mouse embryonic
     fibroblasts (MEFs) derived from FAK-/- and pl30cas-/- mice had severe
     defects in ephrinA1-induced cell spreading, which were reversed
     after re-expression of FAK or pl30cas, resp. Expression of a
     constitutively active EphA2 induced NIH3T3 cells to undergo
     identical, but ligand-independent, morphol. changes. These data show that
     ephrinAl can induce cell adhesion and actin cytoskeletal changes
     in fibroblasts in a FAK- and pl30cas-dependent manner, through activation
     of the EphA2 receptor. The finding that
     ephrin-Eph signalling can result in actin cytoskeletal
     assembly, rather than disassembly, has many implications for
     ephrin-Eph responses in other cell types.
ST
     FAK p130cas ephrina receptor cytoskeletal
     reorganization
IT
     Animal cell line
        (3T3, NIH3T3; FAK and pl30cas in EphrinAl and
        receptors in induction of cytoskeletal reorganization)
IT
     Growth factors, animal
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (EphrinA1; FAK and p130cas in EphrinA1 and
        receptors in induction of cytoskeletal reorganization)
IT
     Adhesion, biological
     Cytoskeleton
     Morphogenesis, animal
        (FAK and p130cas in EphrinA1 and receptors in
        induction of cytoskeletal reorganization)
IT
     Fibroblast
```

```
Microtubule
     Molecular association
        (FAK and p130cas in EphrinAl and receptors in
        induction of cytoskeletal reorganization in relation to)
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (FAK and pl30cas in EphrinAl and receptors in
        induction of cytoskeletal reorganization in relation to)
IT
        (biol.; FAK and pl30cas in EphrinAl and receptors
        in induction of cytoskeletal reorganization)
IT
     Axon
        (outgrowth; FAK and pl30cas in EphrinAl and receptors
        in induction of cytoskeletal reorganization)
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (p125FAK; FAK and p130cas in EphrinA1 and receptors
        in induction of cytoskeletal reorganization)
IT
     Phosphoproteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (p130cas; FAK and p130cas in EphrinA1 and receptors
        in induction of cytoskeletal reorganization)
IT
     Receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (protein, EphrinAl; FAK and pl30cas in
        EphrinA1 and receptors in induction of cytoskeletal
        reorganization)
     144114-16-9, Focal adhesion kinase
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (FAK and pl30cas in EphrinAl and receptors in
        induction of cytoskeletal reorganization)
              THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
(1) Becker, E; Mol Cell Biol 2000, V5, P1537
(2) Berrier, A; J Cell Biol 2000, V151, P1549 HCAPLUS
(3) Bruckner, K; Science 1997, V275, P1640 MEDLINE
(4) Cary, L; J Cell Biol 1998, V140, P211 HCAPLUS
(5) Davy, A; EMBO J 2001, V19, P5396
(6) Davy, A; Genes Dev 1999, V13, P3125 HCAPLUS
(7) Dodelet, V; J Biol Chem 1999, V274, P31941 HCAPLUS
(8) Elowe, S; Mol Cell Biol 2001, V21, P7429 HCAPLUS
(9) Flanagan, J; Annu Rev Neurosci 1998, V21, P309 HCAPLUS
(10) Gao, P; J Neurosci Res 2000, V60, P427 HCAPLUS
(11) Gerlai, R; Nature Rev Neurosci 2001, V2, P205 HCAPLUS
(12) Gonzatti-Haces, M; Proc Natl Acad Sci USA 1988, V85, P21 HCAPLUS
(13) Gu, C; Mol Cell Biol 2001, V14, P4579
(14) Harte, M; Biochim Biophys Acta 2000, V1499, P34 HCAPLUS
(15) Hauck, C; Immunol Res 2000, V21, P293 HCAPLUS
(16) Holland, S; EMBO J 1997, V16, P3877 HCAPLUS
(17) Holland, S; Nature 1996, V383, P722 HCAPLUS
(18) Holmberg, J; Nature 2000, V408, P203 HCAPLUS
(19) Honda, H; Biochem Biophys Res Commun 1999, V262, P25 HCAPLUS
(20) Honda, H; Nature Genet 1998, V19, P361 HCAPLUS
 (21) Huai, J; J Biol Chem 2001, V276, P6689 HCAPLUS
 (22) Huynh-Do, U; EMBO J 1999, V18, P2165 HCAPLUS
 (23) Ilic, D; Nature 1995, V377, P539 HCAPLUS
 (24) Jiang, W; Mol Cell 1998, V2, P877 HCAPLUS
 (25) Klein, R; Curr Opin Cell Biol 2001, V13, P196 HCAPLUS
 (26) Klingbeil, C; J Cell Biol 2001, V152, P97 HCAPLUS
 (27) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
```

(28) Liu, A; Cancer Res 2000, V60, P3429 HCAPLUS (29) Lu, Q; Cell 2001, V105, P69 HCAPLUS (30) Miao, H; Nature Cell Biol 2000, V2, P62 HCAPLUS (31) Miao, H; Nature Cell Biol 2001, V3, P527 HCAPLUS (32) Monschau, B; EMBO J 1997, V16, P1258 HCAPLUS (33) Parsons, J; Oncogene 2000, V19, P5606 HCAPLUS (34) Pasquale, E; Curr Opin Cell Biol 1997, V9, P608 HCAPLUS (35) Pasquale, E; Science 1997, V275, P1640 (36) Polte, T; Proc Natl Acad Sci USA 1995, V92, P10678 HCAPLUS (37) Rodrigues, G; Mol Cell Biol 1993, V13, P6711 HCAPLUS (38) Ruest, P; Cell Growth Differ 2000, V11, P41 HCAPLUS (39) Schlaepfer, D; Mol Cell Biol 1996, V16, P5623 HCAPLUS (40) Schlaepfer, D; Nature 1994, V372, P786 HCAPLUS (41) Schlaepfer, D; Prog Biophys Mol Biol 1999, V71, P435 HCAPLUS (42) Schmucker, D; Cell 2001, V105, P701 HCAPLUS (43) Shamah, S; Cell 2001, V105, P233 HCAPLUS (44) Sieg, D; J Cell Sci 1999, V112, P2677 HCAPLUS (45) Stanzione, R; Lab Invest 2001, V81, P51 HCAPLUS (46) Torring, N; Anticancer Res 2000, V20, P91 HCAPLUS (47) Wahl, S; J Cell Biol 2000, V149, P263 HCAPLUS (48) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS (49) Wilkinson, D; Nature Rev Neurosci 2001, V2, P155 HCAPLUS (50) Yu, H; Oncogene 2001, V20, P3995 HCAPLUS (51) Zhang, Z; Cell 1996, V85, P61 HCAPLUS (52) Zhou, F; J Cell Biol 2001, V153, P1071 HCAPLUS (53) Zisch, A; Oncogene 1998, V16, P2657 HCAPLUS (54) Zou, J; Proc Natl Acad Sci USA 1999, V96, P13813 HCAPLUS L40 ANSWER 36 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN AN 2002:392768 HCAPLUS DN 137:31807 ED Entered STN: 28 May 2002 Antibody targeting of the EphA2 tyrosine TΙ kinase inhibits malignant cell behavior AU Carles-Kinch, Kelly; Kilpatrick, Katherine E.; Stewart, Jane C.; Kinch, Michael S. CS Dep. Basic Med. Sci., Purdue Univ. Cancer Center, West Lafayette, IN, 47907, USA SO Cancer Research (2002), 62(10), 2840-2847 CODEN: CNREA8; ISSN: 0008-5472 PB American Association for Cancer Research DT Journal LA English CC 15-3 (Immunochemistry) AΒ EphA2 is a transmembrane receptor tyrosine kinase that is up-regulated on many aggressive carcinoma cells. Despite its overexpression, the EphA2 on malignant cells fails to bind its ligand, ephrinA1, which is anchored to the membrane of adjacent cells. Unlike other receptor kinases, EphA2 demonstrates kinase activity that is independent of ligand binding. However, ligand binding causes EphA2 to neg. regulate tumor cell growth and migration. Herein, we translate knowledge of EphA2 into strategies that selectively target malignant cells. Using a novel approach to preserve extracellular epitopes and optimize antibody diversity, we generated monoclonal antibodies that

behaviors that are unique to metastatic cells while minimizing damage to

were found to inhibit the soft agar colonization by MDA-MB-231 breast

identify epitopes on the extracellular domain of EphA2.

EphA2 antibodies were selected for their abilities to inhibit

nontransformed cells. A subset of EphA2 monoclonal antibodies

tumor cells but did not affect monolayer growth by nontransformed MCF-10A breast epithelial cells. These EphA2 antibodies also prevented tumor cells from forming tubular networks on reconstituted basement membranes, which is a sensitive indicator of metastatic character. Biochem. analyses showed that biol. active antibodies induced EphA2 phosphorylation and subsequent degradation Antisense-based targeting of EphA2 similarly inhibited soft agar colonization, suggesting that the antibodies repress malignant behavior by down-regulating EphA2. These results suggest an opportunity for antibody-based targeting of the many cancers that overexpress EphA2. Our studies also emphasize how tumor-specific cellular behaviors can be exploited to identify and screen potential therapeutic targets. EphA2 kinase phosphorylation monoclonal antibody

ST cancer

IT Antibodies and Immunoglobulins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(IgG1, monoclonal; antibody targeting of EphA2 tyrosine kinase inhibits malignant cell behavior)

IT Antitumor agents

Cell proliferation

Human

Neoplasm

(antibody targeting of EphA2 tyrosine kinase inhibits malignant cell behavior)

IT Phosphorylation, biological

(protein; antibody targeting of EphA2

tyrosine kinase inhibits malignant cell behavior)

IT 149433-91-0, EphA2 receptor tyrosine

kinase RL: BSU (Biological study, unclassified); BIOL (Biological study) (antibody targeting of EphA2 tyrosine

kinase inhibits malignant cell behavior)

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Bae, S; Breast Cancer Res Treat 1993, V24, P241 MEDLINE
- (2) Bartley, T; Nature (Lond) 1994, V368, P558 HCAPLUS
- (3) Bissell, M; Am J Pathol 1999, V155, P675 MEDLINE
- (4) Cance, W; Breast Cancer Res Treat 1995, V35, P105 HCAPLUS
- (5) Connor, R; Dev Biol 1998, V193, P21 HCAPLUS
- (6) Demicheli, R; Ann Oncol 1997, V8, P1075 MEDLINE
- (7) Devita, V; Cancer:Principles and Practice of Oncology, 5th Edition 1997, P333
- (8) Easty, D; Cancer Res 1995, V55, P2528 HCAPLUS
- (9) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
- (10) Fidler, I; Cancer: Principles and Practice of Oncology, 5th Edition 1997, P135
- (11) Frisch, S; Curr Opin Cell Biol 1997, V9, P701 HCAPLUS
- (12) Fry, D; Curr Opin Biotechnol 1995, V6, P662 HCAPLUS
- (13) Giunciuglio, D; Int J Cancer 1995, V63, P815 HCAPLUS
- (14) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS
- (15) Hunter, T; Cell 1997, V88, P333 HCAPLUS
- (16) Kilpatrick, K; Hybridoma 1995, V14, P355 HCAPLUS
- (17) Kilpatrick, K; Hybridoma 1997, V16, P381 HCAPLUS
- (18) Kilpatrick, K; Hybridoma 1998, V17, P569 MEDLINE
- (19) Kinch, M; Hybridoma 1998, V17, P227 HCAPLUS
- (20) Lawrence, J; World J Urol 1996, V14, P124 MEDLINE
- (21) Levitzki, A; Science (Wash DC) 1995, V267, P1782 HCAPLUS
- (22) Li, L; J Natl Cancer Inst 1989, V81, P1406 MEDLINE

```
(23) Malik, R; Biochim Biophys Acta 1996, V1287, P73 HCAPLUS
(24) Maniotis, A; Am J Pathol 1999, V155, P739 MEDLINE
(25) Mendelsohn, J; Clin Cancer Res 1997, V3, P2703 HCAPLUS
(26) Miao, H; Nature Cell Biol 2000, V2, P62 HCAPLUS
(27) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
(28) Patarca, R; Crit Rev Oncog 1996, V7, P343 HCAPLUS
(29) Pegram, M; J Clin Oncol 1998, V16, P2659 HCAPLUS
(30) Price, J; Breast Cancer Res Treat 1996, V39, P93 MEDLINE
(31) Riethmuller, G; Curr Opin Immunol 1993, V5, P732 MEDLINE
(32) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
(33) Ryu, D; Biotechnol Prog 2000, V16, P2 HCAPLUS
(34) Schlessinger, J; Trends Biochem Sci 1988, V13, P443 HCAPLUS
(35) Sliwkowski, M; Semin Oncol 1999, V26, P60 HCAPLUS
(36) Sutherland, R; Immunol Cell Biol 2001, V79, P49 HCAPLUS
(37) Varmus, H; Introduction Cancer Surv 1986, V5, P153 MEDLINE
(38) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
(39) Weaver, V; Semin Cancer Biol 1995, V6, P175 HCAPLUS
(40) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
(41) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
(42) Zhang, R; Invasion Metastasis 1991, V11, P204 MEDLINE
L40
    ANSWER 37 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2002:361208 HCAPLUS
DN
     137:91669
ED
     Entered STN: 15 May 2002
TT
     Estrogen and Myc negatively regulate expression of the EphA2
     tyrosine kinase
ΑU
     Zelinski, Daniel P.; Zantek, Nicole Dodge; Walker-Daniels, Jennifer;
     Peters, Mette A.; Taparowsky, Elizabeth J.; Kinch, Michael S.
CS
     Department of Basic Medical Sciences, Purdue University Cancer Center,
     West Lafayette, IN, 47907, USA
SO
     Journal of Cellular Biochemistry (2002), 85(4), 714-720
     CODEN: JCEBD5; ISSN: 0730-2312
PB
     Wiley-Liss, Inc.
DT
     Journal
LA
     English
CC
     14-1 (Mammalian Pathological Biochemistry)
     Section cross-reference(s): 2
AR
     Estrogen receptor and c-Myc are frequently overexpressed during
     breast cancer progression but are downregulated in many aggressive forms
     of the disease. High levels of the EphA2 tyrosine
     kinase are consistently found in the most aggressive breast cancer
     cells, and EphA2 overexpression can increase metastatic
     potential. We demonstrate, herein, that estrogen and Myc neg. regulate
     EphA2 expression in mammary epithelial cells. These data reveal
     EphA2 as a downstream target of estrogen and Myc and suggest a
     mechanism by which estrogen and Myc may regulate breast cancer.
ST
     estrogen cMYC EphA2 tyrosine kinase mammary
     epithelium cancer
IT
     Mammary gland, disease
        (benign; estrogen and c-Myc neg. regulate EphA2
        tyrosine kinase expression in mammary epithelial
        cells in relation to breast cancer)
IT
     Transcription factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (c-myc; estrogen and c-Myc neg. regulate EphA2
        tyrosine kinase expression in mammary epithelial
        cells in relation to breast cancer)
IT
     Mammary gland
```

(epithelium; estrogen and c-Myc neg. regulate EphA2

tyrosine kinase expression in mammary epithelial cells in relation to breast cancer)

IT Human

Mammary gland, neoplasm

(estrogen and c-Myc neg. regulate **EphA2 tyrosine kinase** expression in mammary epithelial cells in relation to breast cancer)

IT Estrogen receptors

Estrogens

mRNA

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (estrogen and c-Myc neg. regulate EphA2 tyrosine
 kinase expression in mammary epithelial cells in relation to
 breast cancer)

IT Epithelium

(mammary; estrogen and c-Myc neg. regulate EphA2 tyrosine kinase expression in mammary epithelial cells in relation to breast cancer)

IT Mammary gland, neoplasm

(metastasis; estrogen and c-Myc neg. regulate **EphA2 tyrosine kinase** expression in mammary epithelial cells in relation to breast cancer)

IT 50-28-2, 17β-Estradiol, biological studies 10540-29-1, Tamoxifen
149433-91-0, EphA2 receptor tyrosine
kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (estrogen and c-Myc neg. regulate EphA2 tyrosine
 kinase expression in mammary epithelial cells in relation to
 breast cancer)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Bae, S; Breast Cancer Res Treat 1993, V24, P241 MEDLINE
- (2) Dickson, R; Cancer Treat Res 1992, V61, P249 HCAPLUS
- (3) Dickson, R; Hum Cell 1989, V2, P219 MEDLINE
- (4) Dohn, M; Oncogene 2001, V20, P6503 HCAPLUS
- (5) Dubik, D; Cancer Treat Res 1996, V83, P171 HCAPLUS
- (6) Dubik, D; Oncogene 1992, V7, P1587 HCAPLUS
- (7) Heaney, M; J Virol 1986, V60, P167 HCAPLUS
- (8) Hulka, B; Cancer 1994, V74, P1111 MEDLINE
- (9) Jiang, S; J Natl Cancer Inst 1992, V84, P580 HCAPLUS
- (10) Jordan, V; J Steroid Biochem Mol Biol 2000, V74, P269 HCAPLUS
- (11) Jordan, V; J Toxicol Environ Health 1978, V4, P363 HCAPLUS
- (12) Katzenellenbogen, B; J Steroid Biochem Mol Biol 2000, V74, P279 HCAPLUS
- (13) Kinch, M; J Cell Biol 1995, V130, P461 HCAPLUS
- (14) Krylov, D; Curr Top Microbiol Immunol 1997, V224, P169 HCAPLUS
- (15) Levenson, A; J Steroid Biochem Mol Biol 1994, V51, P229 HCAPLUS
- (16) Macgregor, J; Pharmacol Rev 1998, V50, P151 HCAPLUS
- (17) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
- (18) Osborne, C; Cancer Res 1985, V45, P584 HCAPLUS
- (19) Osborne, M; Ann NY Acad Sci 1999, V889, P146 HCAPLUS
- (20) Peters, M; Mol Cell Biol 1997, V17, P1037 HCAPLUS
- (21) Price, J; Cancer Res 1990, V50, P717 MEDLINE
- (22) Rochefort, H; Ciba Found Symp 1995, V191, P254 HCAPLUS
- (23) Sambrook, J; Molecular cloning:a laboratory manual 1989
- (24) Santos, G; J Biol Chem 1988, V263, P9565 HCAPLUS
- (25) Shiu, R; Clin Chem 1993, V39, P353 HCAPLUS
- (26) Vladusic, E; Oncol Reports 2000, V7, P157 HCAPLUS
- (27) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
- (28) Yardley, D; Am J Med Sci 2000, V320, P263 MEDLINE
- (29) Zajchowski, D; Cancer Res 1993, V53, P5004 HCAPLUS

```
(30) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
(31) Zantek, N; Clin Cancer Res 2001, V7(11), P3640 HCAPLUS
(32) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS
L40
    ANSWER 38 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2002:285562 HCAPLUS
DN
     137:61578
     Entered STN: 17 Apr 2002
ED
ΤI
     Expressed gene sets as markers for specific tumors
IN
     Ramaswamy, Sridhar; Golub, Todd B.; Tamayo, Pablo; Angelo, Michael
PA
     Whitehead Institute for Biomedical Research, USA; Dana-Farber Cancer
     Institute, Inc.
SO
     PCT Int. Appl., 715 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     C12Q001-68
CC
     14-1 (Mammalian Pathological Biochemistry)
     Section cross-reference(s): 3, 9, 63
FAN.CNT 4
     PATENT NO.
                        KIND
                               DATE
                                          APPLICATION NO.
     -----
                        ----
                               -----
                                          -----
                               20020328 WO 2001-XB29287
PΙ
     WO 2002024956
                        A2
                                                                20010919 <--
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BY, BZ, CA, CH, CN, CO,
            CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,
            HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
            LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, RO,
            RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
            VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     WO 2002024956
                               20020328
                                          WO 2001-US29287
                         A2
                                                                  20010919 <--
     WO 2002024956
                         C1
                               20030306
                         А3
                               20030626
     WO 2002024956
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
            PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
            US, UZ, VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
            KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
            GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2000-233534P
                     P
                               20000919
                                         <--
    US 2001-278749P
                         Р
                               20010326 <--
    WO 2001-US29287
                         W
                               20010919 <--
CLASS
               CLASS PATENT FAMILY CLASSIFICATION CODES
WO 2002024956 IC
                       C120001-68
               ECLA
                       C12Q001/68M6B
    Sets of genetic markers for specific tumor classes are described, as well
     as methods of identifying a biol. sample based on these markers. Total
    RNA was isolated from .apprx.300 human tumor and normal tissue specimens
    representing 30 individual classes of tumor or normal tissue, and cDNA
    produced using established mol. biol. protocols was hybridized to two high
    d. Affymetrix oligonucleotide microarrays (Hu6800FL and Hu35KsubA0). Raw
     expression data was combined into a master data set containing the expression
```

values for between 6800 and 16,000 genes expressed by each individual sample. A filter was applied to this data set which only allows those qenes expressed at 3-fold above baseline and with an absolute difference in expression value of 100 to pass. By comparing the sets of genes which are expressed specifically in one class of tumor (e.g., pancreatic adenocarcinoma) vs. its accompanying normal tissue (e.g., normal pancreas), sets of genes were determined which are specific to various tumors and their normal tissue counterparts. Also described are diagnostic, prognostic, and therapeutic screening uses for these markers, as well as oligonucleotide arrays comprising these markers. [This abstract record is one of 4 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.]. gene expression marker tumor diagnosis screening human; bladder tumor gene expression marker; breast tumor gene expression marker; central nervous system tumor gene expression marker; colorectal tumor gene expression marker; endometrial tumor gene expression marker; lung tumor gene expression marker; lymphoma gene expression marker; melanoma gene expression marker; ovarian tumor gene expression marker; pancreas tumor gene expression marker; mesothelioma gene expression marker; prostate tumor gene expression marker; microarray tumor gene expression marker Leukemia (B-cell, acute; expressed gene sets as markers for specific tumors) Leukemia (T-cell, acute; expressed gene sets as markers for specific tumors) Leukemia (acute myelogenous; expressed gene sets as markers for specific tumors) Lung, neoplasm Mammary gland, neoplasm Ovary, neoplasm Pancreas, neoplasm Prostate gland, neoplasm (adenocarcinoma; expressed gene sets as markers for specific tumors) Carcinoma (bladder transitional cell; expressed gene sets as markers for specific tumors) Diagnosis (cancer; expressed gene sets as markers for specific tumors) Nervous system, neoplasm (central; expressed gene sets as markers for specific tumors) Carcinoma Intestine, neoplasm (colorectal adenocarcinoma; expressed gene sets as markers for specific Lymphoma (diffuse large cell; expressed gene sets as markers for specific tumors) Uterus, neoplasm (endometrium, adenocarcinoma; expressed gene sets as markers for specific tumors) DNA microarray technology Drug screening Gene expression profiles, animal Human Leukemia

(expressed gene sets as markers for specific tumors) IT $\ \ \ \mbox{mRNA}$

ST

IT

IT

IT

IT

TT

IT

IT

IT

IT

IT

TΤ

Lymphoma Melanoma Tumor markers

```
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (expressed gene sets as markers for specific tumors)
IT
    Antibodies and Immunoglobulins
    RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (expressed gene sets as markers for specific tumors)
IT
    Gene, animal
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (expressed gene sets as markers for specific tumors)
    Probes (nucleic acid)
IT
    RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (immobilized; expressed gene sets as markers for specific tumors)
IT
     Carcinoma
        (mammary adenocarcinoma; expressed gene sets as markers for specific
        tumors)
IT
    Lung, neoplasm
        (mesothelioma; expressed gene sets as markers for specific tumors)
IT
        (nodular; expressed gene sets as markers for specific tumors)
IT
     Carcinoma
        (ovarian adenocarcinoma; expressed gene sets as markers for specific
        tumors)
IT
     Carcinoma
        (pancreatic adenocarcinoma; expressed gene sets as markers for specific
        tumors)
IT
     Susceptibility (genetic)
        (prediction of; expressed gene sets as markers for specific tumors)
IT
     Carcinoma
        (prostatic adenocarcinoma; expressed gene sets as markers for specific
        tumors)
ΙT
     Carcinoma
        (pulmonary adenocarcinoma; expressed gene sets as markers for specific
        tumors)
IT
     Antitumor agents
        (screening for; expressed gene sets as markers for specific tumors)
IT
    Bladder, neoplasm
        (transitional cell carcinoma; expressed gene sets as markers for
        specific tumors)
IT
     Carcinoma
        (uterine endometrial adenocarcinoma; expressed gene sets as markers for
        specific tumors)
IT
                   134117-62-7
                                 135992-27-7, DNA (human clone BS4.0-H/BS1.3-H
     132749-25-8
     protein HSP 70-Hom gene plus flanks) 136331-58-3 136394-59-7
     139045-39-9, DNA (human gene Hox-1.4 protein cDNA plus 3'-flank)
     139134-78-4, DNA (human clone λhHRC gene HRC coding region plus
               139203-49-9, DNA (human phospholamban cDNA plus flanks)
                   139804-53-8
                                139804-57-2, DNA (human gene CKM)
     139736-13-3
     139804-58-3, DNA (human gene CLG4A)
                                          139804-89-0, GenBank K03008
     139805-07-5, DNA (human gene CYP1A2 coding region plus flanks)
                   139805-41-7, DNA (human gene ELA1 protein cDNA)
     139805-40-6
                  139805-72-4, DNA (human receptor FCRIIa cDNA)
     139805-69-9
     139806-14-7, DNA (human gene IGF2)
                                          139806-50-1, GenBank M16594
     139806-74-9, DNA (human gene HEXB)
                                          139807-18-4, GenBank M27318
     139807-22-0, GenBank M28585
                                   139807-45-7 139808-62-1, DNA (human gene
     SPN cDNA)
                139808-88-1, DNA (human gene MT1F) 139809-28-2
     139809-29-3, DNA (human gene MT1G)
                                         139810-17-6, DNA (human gene PLA2A)
     139810-28-9, DNA (human gene KLK3 cDNA) 139810-70-1, GenBank M32598
     139810-89-2, GenBank M27830
                                   139812-98-9, GenBank M15881
                                                                 139813-00-6,
```

DNA (human gene UMPS cDNA) 139835-99-7, DNA (human gene IGHA1) 139837-38-0 139844-11-4 139847-59-9 139847-73-7, DNA (human gene 139868-64-7 IFN-omega 1) 139848-08-1 139859-21-5 139860-01-8 139949-30-7 140025-51-0, GenBank M19684 140025-64-5, DNA (human gene CHMR4 plus flanks) 140025-75-8, DNA (human gene ADH1) 140026-58-0, GenBank M32373 140026-61-5, DNA (human clone pTR9 satellite 3) 140026-64-8, DNA (human gene ASL cDNA) 140026-92-2, DNA (human gene GLB1 140027-22-1, GenBank X02176 140027-27-6, DNA (human gene CA1 140027-76-5 140027-81-2 140028-29-1 140028-39-3 140028-48-4 140028-62-2, GenBank X07618 140028-96-2 140029-44-3, DNA (human gene G6PD) 140029-53-4, GenBank M11321 140029-92-1 140030-63-3, GenBank M16938 140030-71-3, DNA (human gene 140030-59-7 140031-42-1, GenBank M19169 140031-57-8 140031-79-4 HRG cDNA) 140032-08-2 140032-10-6, GenBank X01059 140032-12-8 140032-40-2 140032-48-0 140032-71-9, DNA (human gene HLA-DQA1 plus flanks) 140032-98-0 140033-49-4, GenBank M36653 140033-52-9, DNA 140032-95-7 (human gene OTC cDNA) 140033-98-3, DNA (human gene PGAM2) 140034-15-7 140034-35-1, GenBank M11726 140034-44-2 140034-78-2 140035-05-8 140035-45-6 140035-79-6, GenBank 140035-19-4, DNA (human gene ACTA1) 140035-96-7 M14158 140035-99-0 140036-02-8, GenBank J05125 140036-41-5, DNA (human 284-amino acid protein 140036-46-0, GenBank M25164 140036-48-2 140036-53-9 140036-68-6, DNA (human protein S cDNA plus flanks) 140048-84-6 140049-62-3, DNA (human adrenodoxin gene) 140051-02-1, DNA (human gene E2B cDNA) 140049-91-8 140063-64-5, DNA (human gene TFPI) 140064-12-6, GenBank M62958 140064-39-7 140068-34-4 140070-32-2, GenBank X52947 140065-45-8 140072-57-7 140072-72-6 140077-15-2, GenBank X17651 140078-75-7, DNA (human gene apoAII) 140078-95-1 140079-19-2 140083-08-5, DNA (human gene CRTM) 140094-77-5, GenBank M76732 140096-68-0, DNA (human gene CTSE) 140108-97-0 140274-50-6 140274-61-9, DNA 140098-98-2 140103-00-0 140274-81-3, DNA (human gene ALDH1) 140275-48-5 (human gene ZNF32) 140275-60-1, DNA (human antithrombin III gene) 140275-96-3 140276-25-1 140276-38-6 140276-49-9 140276-56-8, GenBank X02404 140276-67-1 140276-81-9, DNA (human clone F225 gene COL6A2) 140277-11-8 140277-12-9, GenBank M24400 140277-31-2, GenBank L00389 140277-36-7, DNA (human gene CYP11B1) 140278-41-7 140279-53-4, GenBank M14777 140279-66-9, DNA (human gene H19 fragment) 140279-69-2, GenBank X00038 140279-83-0, DNA (human gene GJA1P1 cDNA) 140280-12-2, GenBank X03794 140280-31-5 140280-39-3, DNA (human gene IVD cDNA) 140280-44-0, DNA (human gene IFNA cDNA) 140281-59-0, GenBank M27749 140281-92-1, 140282-13-9, DNA (human kallikrein cDNA plus flanks) GenBank J00268 140283-19-8, GenBank K01160 140284-23-7, DNA (human gene 140282-35-5 140284-30-6, DNA (human gene NTF3) 140285-25-2, DNA (human prolactin gene) 140285-35-4, DNA (human gene PRB1 cDNA) 140285-75-2, GenBank X00129 140286-04-0 140286-48-2, DNA (human gene ACADS cDNA) 140286-88-0, DNA (human gene TBG cDNA) 140287-46-3, GenBank M29194 140288-21-7, GenBank J03589 140288-63-7, GenBank M26682 140305-79-9, DNA (human gene TRY2 cDNA) 140306-09-8 140317-35-7 140317-82-4 140318-05-4, DNA (human gene MCC cDNA) 140319-36-4 140319-66-0, 140323-51-9 140327-31-7, DNA (human gene MGSA plus GenBank M61855 140327-46-4 140327-49-7 140333-31-9 140333-33-1 flanks) 140333-48-8 140333-60-4 140344-87-2, DNA (human gene HSD11) 140506-26-9, DNA (human gene AR plus flanks) 140353-02-2 140505-97-1 140506-80-5, DNA (human beta-casein cDNA) 140506-84-9, GenBank L00354 140507-62-6, DNA (human gene CLPS cDNA) 140508-14-1, DNA (human gene EL 140508-18-5 140508-28-7 140508-69-6, GenBank M16282 140508-84-5 140508-89-0 140508-95-8, DNA (human gene ITGA2B) 140511-07-5, DNA (human gene inhA) 140511-33-7, DNA (human 140509-48-4 gene KRT16) 140513-38-8 140514-10-9, GenBank X00540 140517-51-7,

```
140538-69-8, GenBank M24248
                                                 140539-49-7, DNA (human
    GenBank K03460
    gene HIS2 cDNA)
                      140738-25-6, DNA (human gene ALDOB plus flanks)
    140738-69-8
                  140738-83-6, DNA (human gene ANT1)
                                                      140740-69-8
                  140741-68-0, GenBank X05309
                                              140741-74-8
    140741-08-8
                                                             140742-53-6
    140742-62-7, DNA (human gene FABP2 plus flanks)
                                                    140743-10-8, DNA (human
    metaxin gene fragment)
                            140743-64-2, DNA (human gene GP1BA) 140743-93-7
    140746-12-9
                  140746-14-1
                               140746-40-3
                                             140748-05-6, DNA (human
    prealbumin gene fragment)
                                140748-26-1
                                              140749-37-7, GenBank M20530
    140750-55-6
                  140750-89-6
                               140750-96-5
                                             140751-97-9
                                                          140752-74-5, DNA
     (human gene F8VWF)
                         140787-65-1, DNA (human gene COL2A1)
                                                               140793-11-9
    140794-60-1, GenBank V00563
                                140796-14-1
                                               140800-01-7 140800-57-3
    140800-71-1
                  140803-99-2
                               140810-76-0
                                             140831-29-4, DNA (human gene
    TFIIE beta cDNA)
                       140831-43-2
                                     140831-68-1, DNA (human gene CPA3)
    140832-44-6
                  140879-44-3
                                140956-86-1, DNA (human gene AK1)
    140961-11-1, GenBank J03764
    RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (nucleotide sequence; expressed gene sets as markers for specific
       tumors)
                  140978-74-1, DNA (human gene C4A)
IT
    140961-24-6
                                                     140983-02-4
                  140985-40-6, GenBank X51954
                                              140997-58-6
    140983-58-0
                                                             140999-65-1, DNA
     (human sperm protein 10 cDNA)
                                   141010-19-7
                                                 141163-75-9
    141165-06-2
                  141657-83-2
                               141657-84-3, DNA (human gene MRC1)
    141659-10-1
                  141706-30-1
                                141878-02-6
                                             142318-64-7
                                                           142361-75-9
                               142789-30-8
     142481-63-8
                  142789-15-9
                                              142789-47-7
                                                          142830-39-5, DNA
     (human gene cdk3 protein kinase cDNA plus flanks)
                 142862-62-2 143001-97-2 143003-24-1, DNA (human clone
    142862-45-1
    HG2-3e defensin isoform 5 gene plus flanks)
                                                143003-34-3
                                                              143283-35-6,
    GenBank X64269
                     143368-19-8 143386-42-9
                                                143388-18-5
                                                             143524-15-6,
                     143695-13-0, DNA (human epithelin cDNA plus flanks)
    GenBank L00972
                 143990-05-0, GenBank X65727 143990-09-4 144014-52-8, DNA
    143787-32-0
     (human chromosome X 1872-nucleotide fragment) 144014-55-1, DNA (human
    gene HOX7 protein cDNA plus flanks)
                                        144014-70-0
                                                      144531-44-2
    144531-47-5
                  144531-48-6
                               144531-69-1
                                             144560-13-4
                                                           144560-31-6
    144560-67-8
                  144590-74-9
                                144755-63-5
                                            145405-51-2
                                                           145495-59-6
                                145711-50-8, DNA (human connexin 37 cDNA plus
    145710-48-1
                  145711-46-2
    flanks)
             145734-31-2
                            145885-48-9
                                         145906-46-3, DNA (human
    arylsulfatase A cDNA)
                            145906-60-1
                                         145906-65-6, DNA (human gene MCL1
            145906-66-7 145906-68-9 145906-69-0, GenBank X51698
    145973-35-9
                  147190-92-9
                                147191-78-4
                                            147825-49-8
                                                           148086-69-5
     148106-92-7
                  148106-94-9
                                148253-81-0
                                            148394-74-5
                                                           148448-81-1, DNA
     (human gene GOS8 plus flanks)
                                   148489-51-4
                                                 148803-09-2, GenBank X69699
     148958-71-8
                  148958-80-9
                               149239-81-6
                                             149278-23-9
                                                          149309-67-1, DNA
     (human retinoic acid receptor isoform \gamma7
     fragment-specifying) 149318-04-7 149348-71-0
                                                     149702-48-7
                  149800-67-9
     149738-21-6
                                149801-72-9
                                            150003-43-3 150219-16-2
    150219-72-0
                               150219-97-9, DNA (human clone gES-6 peptide YY
                  150219-73-1
                       150247-53-3
                                    150326-43-5
                                                  150421-29-7, DNA (human
    gene plus flanks)
    gene PCK1 plus flanks) 150488-75-8, DNA (human gene C6)
                                                              150489-55-7
    150498-65-0
                  150510-74-0
                                             150574-93-9
                                                           150755-01-4
                                150510-91-1
    150861-12-4
                  150861-19-1
                               150862-92-3
                                             150912-14-4
                                                           150946-37-5,
    GenBank X68994
                     151210-94-5
                                  151212-76-9
                                                151242-00-1
                                                             151279-88-8
    151315-23-0, GenBank L23852
                                  151318-00-2
                                              151318-04-6
                                                             151319-18-5
                  151350-69-5
                                151430-26-1
                                            151431-95-7
                                                           151469-96-4
    151350-66-2
    151470-00-7
                  151471-49-7
                                151494-19-8
                                            151550-24-2
                                                           151576-51-1
    151576-70-4
                  151576-92-0, DNA (human gene N-cym protein cDNA
    plus flanks)
                  151580-68-6 151612-44-1 151658-42-3, DNA (human
    connexin 40 gene plus flanks) 151661-32-4 151784-77-9
                                                              152002-67-0
    152281-24-8 152283-42-6 152317-60-7 152345-13-6 152345-14-7
     152347-85-8, DNA (human gene HRY plus flanks)
                                                 152392-99-9 152395-29-4
```

```
152412-16-3, DNA (human gene ACT)
                                        152649-01-9
                                                      152649-54-2
                                153054-80-9
                                             153054-97-8
    152652-52-3
                  153016-86-5
                                                            153317-44-3
    153317-49-8
                  153378-26-8
                                153592-40-6
                                              153676-66-5
                                                            153768-41-3
                                              154298-73-4
    153961-88-7
                  153965-35-6
                                154209-03-7
                                                            154298-74-5
    154610-29-4
                  154834-82-9
                                154898-86-9
                                              154899-11-3
                                                            154901-48-1
    154983-49-0
                  154996-23-3
                                154997-64-5
                                              155119-73-6
                                                            155120-27-7
    155316-75-9
                  155356-21-1 155458-29-0
                                              155459-85-1
                                                            155465-87-5
    155483-28-6
                  155744-38-0
                                156195-86-7
                                              156224-31-6
                                                            156225-25-1,
    GenBank D17570
                     156253-81-5
                                   156584-20-2
                                                 156584-21-3
                                                               156588-04-4
    156652-81-2
                                156675-03-5
                                              156678-99-8
                                                            156712-17-3
                  156653-52-0
                                156889-18-8
                                              156889-70-2
                                                            156889-72-4
    156797-53-4
                  156830-46-5
    156890-31-2, DNA (human gene MSP)
                                       158024-71-6
                                                      158086-18-1
                                158127-74-3
                  158108-96-4
                                             158158-57-7
                                                            158158-70-4
    158108-72-6
                                158209-90-6, GenBank U13680
    158159-47-8
                  158160-23-7
                                                            158245-55-7
    158246-12-9
                  158278-53-6
                                158450-99-8
                                             158480-69-4
                                                            158645-88-6
    158683-87-5
                  158683-88-6
                                158761-48-9
                                              158764-50-2
                                                            159069-23-5
                                160020-24-6
                                              160021-32-9
    159348-11-5
                  159994-88-4
                                                            160042-15-9
    160075-49-0
                  160077-60-1
                                160102-96-5
                                              160104-14-3
                                                            160120-60-5
    160122-16-7
                  160220-21-3
                                160364-89-6
                                              160475-68-3
                                                            160475-72-9
                                160864-85-7, DNA (human clone Q1 cDNA)
    160475-73-0
                  160475-87-6
     160897-69-8
                                161046-30-6
                                              161048-39-1, GenBank U12622
                  160930-90-5
     161072-97-5
                                161343-14-2
                  161164-15-4
    RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (nucleotide sequence; expressed gene sets as markers for specific
        tumors)
TΤ
    161351-22-0
                                161413-23-6
                                              161413-51-0
                                                            161413-52-1
                  161413-21-4
                                161784-15-2, DNA (human gene CAMLG cDNA)
     161657-05-2
                  161657-67-6
                  162485-91-8
                                162527-66-4
                                              162596-05-6
                                                            163048-43-9
     162198-09-6
     163199-97-1
                  163239-69-8
                                163245-09-8
                                              163246-34-2
                                                            163246-42-2
     163246-61-5
                  163247-65-2
                                163249-81-8
                                              163377-47-7
                                                            163792-22-1
     163872-84-2, DNA (human gene MIA plus flanks)
                                                  163953-69-3, DNA (human
    gene AVPR1A plus flanks) 164000-06-0 164272-34-8, DNA (human clone
    pbeta1RT1 cDNA)
                      164373-62-0
                                   164478-51-7 164478-54-0
                                                                164479-07-6
     164479-11-2, DNA (human clone PEP11 (RT-PCR) cDNA) 164568-03-0
                  164598-61-2 164751-20-6
                                              164843-43-0
                                                            164952-31-2
     164598-54-3
                                164968-01-8
                  164953-07-5
                                              165025-17-2
                                                            165148-42-5
     164952-57-2
                  165212-95-3
                                165296-69-5
                                              165367-11-3
                                                            165437-24-1
     165205-99-2
                                165472-96-8
                                              165473-04-1, DNA (human clone R4
                  165471-19-2
     165471-10-3
                      165474-49-7 165497-11-0
                                                  165500-22-1, DNA (human gene
        165474-30-6
                                           165624-09-9, DNA (human clone A23 )
    LMO4 autoantigen cDNA) 165567-43-1
                                165765-87-7
                                              165850-77-1
     165706-55-8
                  165718-13-8
                                                            165912-14-1
                  166012-39-1
                                166071-00-7
                                              166136-57-8
     165981-92-0
                                                            166215-00-5
     166222-27-1
                  166224-96-0
                                166292-03-1
                                              166299-97-4
                                                            166349-36-6
                                                   166357-76-2
     166357-11-5, DNA (human alpha s1 casein cDNA)
                                                                  166357-81-9,
     DNA (human LI-cadherin cDNA) 166363-36-6 166416-55-3
                                                              166424-16-4
     166427-47-0 166428-94-0 166456-53-7 166643-02-3
                                                           166840-26-2
     166841-75-4, DNA (human DNA-binding protein cDNA)
                                                      166846-13-5,
     DNA (human clone c51 ) 166926-59-6, DNA (human syntaxin 5 cDNA plus
             166926-84-7
                            167054-46-8 167056-35-1 167176-95-6
     flanks)
     167206-77-1, DNA (human cell line TE671 cDNA) 167246-69-7
                                                                  167519-36-0
                  167711-40-2 167711-89-9, DNA (human cell line HL-60, Y-79
     167599-64-6
     cDNA)
            167712-54-1 167712-81-4
                                       167713-04-4, DNA (human Hel-N2 cDNA)
                                167714-27-4
                  167714-16-1
                                              167714-31-0
                                                            168043-01-4
     167713-42-0
                  168313-53-9
                                              168374-75-2
     168312-02-5
                                168364-88-3
                                                            168380-68-5
                                168385-98-6
     168380-90-3
                  168381-65-5
                                              168389-88-6
                                                            168437-24-9
                                              168490-70-8
     168437-64-7
                  168441-08-5
                                168444-00-6
                                                            168491-32-5
                                168494-93-7
     168493-92-3
                  168494-73-3
                                              168512-67-2, GenBank X90579
                                168597-11-3
                  168523-60-2
     168514-53-2
                                              168601-82-9
                                                           168605-05-8
                                              168665-23-4, DNA (human RIG cDNA
     168605-09-2
                  168654-84-0
                                168658-56-8
```

```
plus flanks)
               168802-17-3
                             168857-47-4
                                           168857-68-9
                                                         168882-67-5
168929-53-1
              168938-52-1
                            168947-93-1
                                          169023-34-1
                                                        169071-49-2
169087-30-3, DNA (human osteopontin gene fragment)
                                                    169091-84-3
                                          169733-38-4, DNA (human gene IP)
169629-63-4
              169630-52-8
                            169717-12-8
170274-35-8
              170319-36-5
                            170322-31-3
                                          170335-10-1
                                                        170339-03-4
                            170536-78-4
170339-05-6
              170402-97-8
                                          170558-15-3
                                                        170592-00-4
170611-55-9
              170676-15-0
                            170778-52-6
                                          170896-07-8
                                                        171026-03-2
171091-37-5
              171136-58-6
                            171150-53-1
                                          171152-59-3
                                                        171166-35-1
171166-38-4
              171212-61-6
                            171449-28-8
                                          171546-17-1
                                                        171639-70-6, DNA
(human gene UNR plus flanks)
                               171690-41-8
                                             171845-09-3
                                                           171845-17-3,
DNA (human cell line KG-1 cDNA)
                                  171845-35-5
                                                171845-37-7, DNA (human
cell line KG-1 cDNA)
                       171845-41-3, DNA (human cell line KG-1 cDNA)
171871-43-5
              171940-42-4, GenBank M29037
                                            172000-16-7
                                                          172013-21-7
172013-51-3
              172013-60-4
                            172013-63-7
                                          172131-71-4
                                                        172137-40-5
172176-14-6
              172177-78-5
                            172186-02-6
                                          172249-69-3
                                                        172380-30-2
172386-39-9
              172444-61-0
                            172447-27-7
                                          172627-97-3
                                                        172628-01-2
172640-29-8
              172764-79-3
                            172866-06-7
                                          173003-32-2
                                                        173005-29-3,
GenBank U44848
                 173077-58-2
                               173124-35-1
                                             173126-01-7
                                                           173128-98-8
173130-87-5
             173183-19-2 173231-04-4 173233-10-8
                                                       173234-86-1,
GenBank D82373
                 173487-64-4
                               173573-29-0 173661-84-2
                                                          173661-86-4
173708-75-3, DNA (human clone jj1b cDNA) 173753-96-3
                                                         173758-66-2, DNA
(human gene HD-6 plus flanks)
                                173889-20-8
                                              173891-43-5, DNA (human
cadherin 15 cDNA plus flanks)
                                173891-44-6
                                              173893-06-6
                                                            173893-10-2
173968-70-2
              174057-07-9
                            174121-27-8
                                          174124-42-6
                                                        174127-56-1
174286-76-1
              174287-31-1
                            174388-39-7
                                          174441-90-8, DNA (human clone
#48ES4 cDNA)
               174442-85-4 174478-15-0
                                          174518-29-7
                                                         174820-89-4
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
   (nucleotide sequence; expressed gene sets as markers for specific
   tumors)
174821-80-8, DNA (human gene MDS1 cDNA)
                                          175001-00-0
                                                        175004-10-1, DNA
(human mariner element Hsmar2)
                                 175004-94-1
                                              175007-63-3, DNA (human
gene HNMT exon 6 plus flanks)
                                175008-17-0
                                              175038-06-9
                                                            175040-79-6
                            175108-24-4
                                          175113-05-0, DNA (human gene
175045-42-8
              175107-65-0
pCP-2 cDNA)
              175122-87-9
                            175127-18-1
                                          175129-42-7
                                                        175196-96-0, DNA
(human GABAA receptor alpha3)
                                175270-48-1, GenBank U51010
175270-64-1
              175270-71-0, GenBank U51711 175299-02-2, DNA (human gene
MKP-2 cDNA)
              175381-75-6
                           175383-02-5 175383-10-5
                                                        175383-19-4,
GenBank D83847
                 175421-00-8
                               175421-01-9
                                             175515-51-2
                                                           175524-88-6
```

175754-72-0 175828-04-3 175928-92-4 176145-57-6 176183-77-0 176188-90-2 176195-25-8 176339-56-3 176345-91-8 176348-12-2, DNA 176348-17-7 176355-91-2, GenBank W26769 (human gene Doc1) 176356-16-4, GenBank W25869 176359-14-1 176361-43-6 176362-81-5 176363-64-7, GenBank W27176 176393-37-6 176393-77-4, GenBank W26360 176401-66-4 176397-59-4 176401-49-3, GenBank W27650 176402-33-8 176403-65-9, GenBank W27857 176402-72-5 176406-30-7, GenBank W28151 176406-45-4, GenBank W28229 176406-85-2, GenBank W27993 176407-55-9, GenBank W28252 176416-47-0 176428-38-9 176459-47-5 176464-52-1 176471-15-1 176520-97-1 176591-89-2 176603-67-1 176604-45-8 176630-77-6, DNA (human gene AQP5) 176613-34-6 176630-28-7 176740-71-9 176800-07-0, DNA (human gene RACH1 cDNA) 176883-39-9 177253-81-5 177301-21-2 177305-13-4 177372-86-0 177511-10-3 177632-12-1 177630-36-3 177643-37-7 177644-01-8 177693-62-8 177823-29-9 177891-87-1 177823-24-4 177929-43-0 178010-74-7 178083-79-9 178148-59-9 178148-81-7 178149-57-0 178150-00-0 178195-02-3 178188-24-4 178295-02-8 178295-03-9 178298-60-7 178300-49-7 178410-26-9 178639-38-8 178642-69-8 178642-90-5 178644-08-1 178647-66-0 178653-29-7 178653-38-8 178655-85-1 178734-25-3 178842-70-1 178848-89-0, DNA (human gene 178658-99-6 178850-44-7 LIMK1 plus flanks) 178850-79-8 178850-95-8 178851-16-6 178892-10-9

178851-92-8

IT

178852-84-1

179194-94-6

179227-13-5

```
179423-99-5
179227-53-3
              179299-57-1
                            179308-32-8
                                                         179442-95-6
              179501-27-0
                                           179582-14-0
                                                         179592-96-2
179443-08-4
                            179576-58-0
                                           179710-24-8
179644-49-6
              179645-72-8
                            179709-58-1
                                                         179719-00-7
                                           179780-03-1
179727-11-8
              179773-35-4
                            179773-78-5
                                                         179787-01-0
179790-80-8
              179827-57-7
                            179843-39-1
                                           179955-63-6
                                                         179956-88-8, DNA
(human rhodopsin kinase cDNA)
                                 179965-66-3
                                               180013-00-7
180015-38-7
              180026-61-3
                            180108-80-9, DNA (human \delta-sarcoglycan
        180109-04-0
                      180118-30-3
                                     180121-08-8
                                                   180173-27-7
180223-46-5
              180228-09-5
                            180245-62-9
                                           180245-67-4
                                                         180245-69-6
              180362-95-2
                           180375-77-3
                                           180376-08-3
                                                         180377-54-2
180362-85-0
180379-03-7
              180380-57-8
                            180426-24-8
                                           180446-01-9
                                                         180448-36-6, DNA
(human gene KIAA0233 cDNA fragment)
                                      180448-88-8, DNA (human gene
                          180452-77-1
                                        180454-95-9
                                                       180456-19-3
KIAA0240 cDNA fragment)
                            180456-71-7
                                           180459-79-4
                                                         180505-81-1
180456-32-0
              180456-65-9
180547-53-9
              180549-97-7
                            180552-01-6
                                           180566-57-8
                                                         180604-89-1
                            180654-68-6
                                           180672-28-0, DNA (human clone
180653-54-7
              180654-08-4
161455-2-3 cDNA)
                   180672-32-6, DNA (human clone W2-6 cDNA)
                                                               180674-18-4
                            180752-84-5
                                           180755-70-8
                                                         180756-89-2
180674-69-5
              180701-76-2
                            180771-34-0, DNA (human gene CGM2 cDNA)
180762-53-2
              180769-47-5
              180884-37-1, DNA (human clone 80578 )
                                                       180924-05-4, GenBank
180882-94-4
                       181087-79-6
                                     181091-83-8
                                                    181095-22-7
U67614
         181087-60-5
181101-34-8
              181102-54-5
                            181105-48-6
                                           181105-75-9, GenBank U68494
181109-06-8, DNA (human imogen 38 cDNA)
                                           181159-60-4
                                                         181165-98-0
              181172-09-8
                            181172-35-0
                                           181196-56-5
                                                         181201-49-0
181168-12-7
                                                           181290-25-5
181203-31-6
              181254-90-0, DNA (human gene ASML3a cDNA)
                                                         181555-01-1
181291-67-8
              181320-58-1
                            181392-46-1
                                           181545-26-6
181555-18-0
              181568-46-7
                            181613-43-4
                                           181617-56-1
                                                         181670-57-5
181687-64-9
              181688-54-0
                            181726-44-3
                                           181861-24-5, DNA (human gene
                                     181918-38-7
VASP)
       181861-25-6
                      181909-41-1
                                                   181922-15-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
   (nucleotide sequence; expressed gene sets as markers for specific
   tumors)
                             182113-82-2
                                           182335-57-5
                                                         182342-28-5, DNA
181922-26-9
              182099-03-2
                              182378-06-9
                                             182391-43-1
                                                           182445-45-0
(human clone EST90757 cDNA)
                            182649-02-1, GenBank AA093748
182544-30-5
              182589-34-0
                                                              182659-46-7
182667-45-4, GenBank AA095600
                                 182726-09-6
                                               182726-30-3
                                                              182736-53-4
182762-41-0, DNA (human cell line KD cDNA)
                                              182774-82-9
                                                             182791-83-9
                                           182860-92-0
                                                         182911-68-8
182793-34-6
              182858-93-1
                             182860-63-5
              183080-65-1
                             183100-32-5
                                           183100-37-0
                                                          183100-52-9
182942-52-5
              183192-26-9, DNA (human cell line Hela clone C3 cDNA)
183100-56-3
183329-51-3
              183331-35-3
                            183390-79-6
                                           183390-81-0
                                                         183391-54-0
              183453-57-8
                             183458-20-0
                                           183463-13-0
                                                          183631-56-3
183391-55-1
              183640-19-9
                             183644-77-1
                                           183686-19-3
                                                          183687-95-8
183632-34-0
              183697-65-6
183693-30-3
                             183709-87-7.
                                           183753-26-6
                                                          183771-66-6
                             183777-80-2
183772-72-7
              183773-24-2
                                           183779-07-9
                                                          183781-34-2, DNA
(human gene nbr cDNA) 183820-63-5
                                       183820-77-1
                                                    183821-69-4
                             183829-61-0
183823-87-2
              183827-60-3
                                           183842-16-2
                                                         183844-41-9
                             183976-79-6
                                           183976-88-7, DNA (human clone
              183976-71-8
183845-08-1
RACE clone A3 cDNA)
                      183983-92-8
                                     183984-22-7
                                                   183984-25-0
                             184054-27-1
                                           184076-34-4
                                                          184076-44-6
183984-37-4
              183984-43-2
                             184142-89-0
                                           184145-33-3
                                                          184188-09-8
184136-65-0
              184141-74-0
              184208-77-3
                             184251-20-5
                                           184255-05-8
                                                          184261-63-0
184200-93-9
184320-57-8
              184321-89-9
                             184322-47-2
                                           184323-85-1
                                                          184325-25-5
              184332-16-9
                             184333-06-0
                                           184333-86-6
                                                          184334-25-6
184329-92-8
184334-37-0
              184339-82-0
                             184342-71-0
                                           184343-23-5
                                                          184381-27-9
              184391-26-2
                           184398-52-5
                                           184412-45-1
                                                          184414-01-5
184383-01-5
              184512-11-6
                             184610-03-5
                                           184611-54-9
                                                          184660-11-5, DNA
184501-15-3
(human gene GPR23 plus flanks)
                                  184665-25-6
                                                184672-66-0, DNA (human
```

```
gene DDR fragment)
                     184673-20-9
                                    184750-98-9
                                                   184753-67-1
                                                                 184860-63-7
184860-93-3
              184862-66-6
                             184864-12-8
                                          184864-45-7
                                                          184974-91-2, DNA
(human gene HXC-26 cDNA)
                            184976-07-6
                                          185008-36-0
                                                         185079-43-0
185080-80-2
              185083-60-7
                             185083-66-3, DNA (human gene RFB30 plus
flanks)
          185176-44-7
                        185179-13-9
                                       185231-24-7, GenBank D17357
185239-96-7
              185242-26-6
                             185243-06-5
                                           185270-20-6
                                                          185273-85-2
185277-62-7
              185294-66-0
                             185354-34-1
                                           185359-89-1
                                                          185367-32-2
185369-23-7
              185370-07-4
                             185374-59-8
                                           185374-60-1
                                                          185374-63-4
                             185634-65-5
185474-11-7
              185481-52-1
                                           185649-22-3
                                                          185650-14-0
185665-75-2
              185725-38-6
                             185770-09-6, DNA (human gene DDR3 cDNA)
185770-11-0, GenBank U83600
                               185773-76-6
                                             185782-56-3
                                                            185796-18-3
185835-35-2
              185866-67-5
                             185941-84-8
                                           185973-37-9
                                                          186007-73-8
              186017-51-6, DNA (human clone CTA-322B1 )
186015-45-2
                                                            186220-65-5
186226-71-1, DNA (human YF5 cDNA)
                                     186292-18-2
                                                   186363-68-8
186363-70-2, DNA (human clone cosmid W12A)
                                               186403-86-1, DNA (human
clone IMAGE: 74593 cDNA)
                           186404-15-9
                                         186445-82-9, DNA (human clone
                                                       186445-95-4
151B14 )
           186445-90-9
                         186445-92-1
                                        186445-94-3
186487-30-9
              186514-41-0
                             186622-12-8
                                           186626-67-5
                                                          186626-84-6
186627-43-0
              186628-68-2
                             186630-43-3
                                           186631-53-8
                                                          186631-94-7
186633-74-9
              186633-86-3
                             186637-50-3
                                           186638-06-2
                                                          186681-64-1
186786-14-1
              186853-21-4
                             186855-00-5
                                           186858-50-4
                                                          186861-17-6
186862-21-5
              186862-25-9
                             186862-73-7
                                           186864-26-6
                                                          186867-49-2
186868-08-6
              186868-27-9
                             186868-96-2
                                           186871-37-4
                                                          186871-49-8
186872-72-0
              186873-06-3
                             186876-27-7
                                           186876-43-7
                                                          186877-98-5
186878-08-0
              186878-12-6
                             186879-33-4
                                           186880-87-5
                                                          186881-39-0
                                           186999-64-4
186881-94-7
              186926-14-7
                             186930-73-4
                                                          187002-78-4
187192-53-6
              187193-78-8
                             187201-28-1
                                           187202-54-6
                                                          187202-57-9
187204-27-9
              187310-20-9, DNA (human EST (expressed sequence tag))
187317-03-9
              187322-19-6
                             187363-69-5
                                           187366-15-0
                                                          187366-80-9
187366-81-0
              187367-20-0
                             187367-99-3
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
   (nucleotide sequence; expressed gene sets as markers for specific
   tumors)
187368-12-3
              187368-61-2
                             187370-83-8
                                           187373-02-0
                                                          187375-40-2
187383-99-9
              187384-46-9
                             187384-53-8
                                           187439-06-1
                                                          187501-10-6
187501-51-5, DNA (human gene CLDN10 cDNA)
                                             187508-85-6
                                                            187508-91-4
187509-94-0
              187510-03-8
                             187511-11-1
                                           187512-24-9
                                                          187514-64-3
187515-70-4
              187515-95-3
                             187517-03-9
                                           187517-73-3
                                                          187558-47-0
187559-20-2
              187560-75-4
                             187561-20-2
                                           187563-30-0
                                                          187565-73-7
187637-02-1
              187638-15-9
                             187646-94-2
                                           187647-01-4
                                                          187651-91-8
                                           188089-55-6, DNA (human clone
187767-39-1
              187821-70-1
                             188013-72-1
23574 cDNA)
              188089-61-4, DNA (human clone 23652 cDNA)
                                                            188089-63-6, DNA
                            188089-64-7, DNA (human clone 23587 cDNA)
(human clone 23665 cDNA)
188164-01-4
              188164-46-7
                             188169-81-5
                                           188212-32-0
                                                          188212-56-8
188218-22-6
              188219-78-5, DNA (human gene GCP-2 plus flanks)
188219-95-6, GenBank U90065
                               188221-65-0
                                             188223-27-0
                                                            188223-98-5
                                           188238-49-5
              188232-71-5
                             188236-84-2
188226-28-0
                                                          188268-21-5
188268-96-4
              188270-08-8
                             188274-68-2
                                           188275-20-9
                                                          188275-44-7
188279-60-9
              188280-84-4
                             188282-76-0
                                           188312-24-5
                                                          188312-52-9
188313-12-4
              188314-17-2
                             188314-35-4
                                           188320-52-7
                                                          188321-50-8
188337-72-6
              188379-53-5
                             188453-46-5
                                           188455-73-4
                                                          188456-18-0
              188460-73-3
                             188463-48-1
188458-24-4
                                           188469-84-3
                                                          188470-68-0
188902-60-5
              188963-18-0
                             188963-28-2
                                           188963-39-5
                                                          188963-40-8
              189356-93-2, DNA (human villin-like protein cDNA)
189123-94-2
189357-12-8
              189404-82-8
                             189405-99-0
                                           189409-21-0
                                                          189409-23-2
189413-94-3
              189417-48-9
                             189420-63-1
                                           189420-76-6
                                                          189422-50-2
189422-72-8
              189423-86-7
                             189428-16-8
                                           189428-91-9
                                                          189430-29-3
189430-73-7
              189433-53-2
                             189436-17-7
                                           189436-24-6
                                                          189436-25-7
189436-35-9
              189463-46-5, DNA (human sarcolipin cDNA plus flanks)
```

189608-35-3

189708-66-5

189608-25-1

189520-90-9

189605-37-6

```
189711-23-7
                   189712-34-3
                                 189714-59-8
                                                189715-43-3
                                                              189717-96-2
                                 189740-49-6
                                                189772-05-2
     189724-23-0
                   189725-80-2
                                                              189775-04-0, DNA
                                 189775-52-8, DNA (human gene ATP2A1 plus gene
     (human clone 143789 cDNA)
               189776-69-0
                             189778-15-2
                                          189778-41-4
                                                          189787-55-1
     ATP2A1)
                                 189803-64-3
     189789-83-1
                   189792-25-4
                                                189834-17-1
                                                              189834-25-1
     189837-40-9
                   189838-31-1
                                 189838-39-9
                                                189900-85-4
                                                              189905-42-8
     189907-87-7
                   189910-84-7
                                 189912-32-1
                                                189912-67-2
                                                              189914-28-1
     189917-18-8
                   189920-83-0
                                 189920-96-5
                                                189922-29-0
                                                              189923-58-8
     189968-08-9
                   189970-13-6
                                 189971-97-9
                                                189973-74-8
                                                              189974-10-5
     190029-43-7
                   190030-49-0
                                 190031-22-2
                                                190033-61-5
                                                              190036-06-7
     190115-84-5
                   190116-83-7
                                 190116-94-0
                                                190145-63-2
                                                              190147-16-1
     190155-82-9
                   190157-23-4
                                 190157-32-5
                                                190162-34-6
                                                              190162-68-6
     190163-13-4
                   190171-19-8
                                 190179-81-8
                                                190180-29-1, DNA (human clone
     cosGT13 )
                 190427-21-5
                               190427-42-0
                                              190429-68-6
                                                          190478-36-5
     190478-50-3
                   190495-68-2
                                 190497-54-2
                                                190497-65-5
                                                              190498-30-7
                   190503-71-0
                                                190556-71-9
     190500-22-2
                                 190552-38-6
                                                              190558-67-9
     190558-85-1
                   190563-54-3
                                 190565-67-4
                                                190566-78-0
                                                              190571-51-8
     190622-42-5
                   190630-84-3
                                 190631-13-1
                                                190637-75-3
                                                              190641-30-6
     190641-39-5
                   190644-75-8
                                 190680-04-7
                                                190682-30-5
                                                              190682-50-9
     190682-61-2
                   190683-22-8
                                 190684-22-1
                                                190696-85-6
                                                              190696-86-7
     190697-19-9
                   190697-67-7
                                 190698-30-7
                                                190698-73-8
                                                              190701-66-7
                   190817-63-1
                                 190821-88-6
                                                190822-04-9
                                                              190822-05-0
     190816-26-3
     190823-71-3
                   190825-00-4
                                 190867-20-0
                                                190868-32-7
                                                              190868-69-0
     190868-77-0
                                 190875-87-7
                                                190876-69-8
                   190873-29-1
                                                              190878-16-1
                   190882-69-0
                                 190883-74-0
                                                190894-24-7
     190882-34-9
                                                              190920-39-9, DNA
                                       190920-95-7, DNA (human P2x purinoceptor
                        190920-46-8
     (human gene FLII)
             190921-05-2, DNA (human cell line WI-38 cDNA)
                                                              190984-65-7
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (nucleotide sequence; expressed gene sets as markers for specific
        tumors)
IT
     190987-31-6
                   190989-34-5
                                 191001-62-4
                                                191004-16-7
                                                              191007-62-2
     191008-78-3
                   191009-25-3
                                 191011-45-7
                                                191047-87-7
                                                              191048-19-8
                   191048-37-0
                                                              191073-34-4
     191048-28-9
                                 191071-42-8
                                                191072-62-5
     191073-80-0
                   191074-44-9
                                 191081-18-2
                                                191081-36-4
                                                              191081-56-8
                   191117-94-9
                                 191120-11-3
     191116-45-7
                                                191120-61-3
                                                              191121-47-8
                                 191125-74-3
     191122-84-6
                   191123-64-5
                                                191125-91-4
                                                              191128-35-5
                   191132-84-0
     191132-23-7
                                 191138-44-0
                                                191140-30-4
                                                              191141-51-2
     191143-53-0
                   191144-35-1
                                 191145-30-9
                                                191145-71-8
                                                              191146-63-1
                                                              191196-38-0
     191147-28-1
                   191188-90-6
                                 191190-87-1
                                                191192-59-3
     191198-21-7
                   191200-90-5
                                 191239-28-8
                                                191240-08-1
                                                              191246-78-3
     191249-18-0
                   191257-53-1
                                 191259-52-6
                                                191262-30-3
                                                              191263-05-5
                   191271-10-0
     191263-09-9
                                 191292-11-2
                                                191315-69-2
                                                              191318-36-2
     191366-90-2
                   191367-08-5
                                 191368-31-7
                                                191373-86-1
                                                              191375-78-7
     191376-47-3
                   191378-03-7
                                 191394-60-2
                                                191438-50-3
                                                              191439-90-4
                                                191459-25-3
                                                              191459-62-8
     191440-26-3
                   191451-85-1
                                 191458-69-2
     191629-68-2
                   191751-48-1, GenBank AA335018
                                                    191826-57-0, GenBank
                191832-60-7, GenBank AA340539
                                                 191889-75-5
                                                               191897-30-0
     AA340065
     191954-08-2
                   191962-53-5
                                 191968-55-5
                                                191973-52-1, GenBank AA348466
     192020-92-1, GenBank AA350030
                                     192143-29-6
                                                    192143-49-0
                                                                  192143-58-1
                                 192168-08-4, GenBank AA358147
     192143-77-4
                   192143-87-6
                                                                  192175-18-1,
                        192289-52-4
                                      192304-27-1
     GenBank AA358888
                                                     192399-66-9, GenBank
     AA370353
               192416-01-6
                             192422-64-3
                                           192474-49-0
                                                          192498-48-9
                                 192563-32-9
     192502-25-3
                   192534-62-6
                                                192605-62-2, GenBank AA381902
     192670-32-9
                   192856-31-8
                                 192856-45-4, DNA (human clone RP3-452H17 )
                                 192957-70-3
     192955-77-4
                   192955-99-0
                                                192958-61-5
                                                              192962-55-3
     192965-03-0
                   192966-31-7
                                 192968-09-5
                                                192985-36-7
                                                              193028-84-1
     193029-18-4
                   193029-76-4
                                 193030-10-3
                                                193030-13-6
                                                              193030-87-4
     193033-15-7
                   193036-65-6
                                 193039-14-4
                                                193039-87-1
                                                              193041-33-7
```

193108-36-0

193110-39-3

193108-03-1

193042-70-5

IT

193043-91-3

```
193134-75-7, GenBank Y13896
                             193164-23-7
                                          193164-88-4
                                                        193165-82-1
193172-20-2
             193174-62-8
                           193186-20-8 193189-73-0
                                                      193191-34-3
193193-11-2
             193230-42-1
                           193235-91-5
                                         193236-42-9
                                                      193238-07-2
193238-61-8
             193238-89-0
                           193246-30-9 193246-86-5
                                                      193250-38-3
             193257-52-2 193258-30-9
193251-25-1
                                       193258-32-1
                                                      193261-38-0
193375-10-9
             193398-38-8
                         193449-29-5, GenBank AA299655
                                                           193517-28-1
193523-61-4
             193579-83-8 193601-30-8
                                        193716-50-6
                                                      193732-40-0
193734-60-0
             193785-25-0
                          193865-24-6
                                         193880-28-3
                                                       193932-08-0
193933-07-2
             193933-75-4
                          193934-18-8
                                         193934-21-3
                                                       193935-95-4
193937-44-9
             193942-90-4
                          193943-27-0
                                         193943-56-5
                                                      194004-80-3
194133-39-6
             194134-31-1 194136-96-4
                                         194138-47-1
                                                      194330-40-0, DNA
(human gene RGS3 cDNA) 194331-29-8, DNA (human cadherin FIB1 cDNA)
194331-30-1, DNA (human cadherin FIB2 cDNA)
                                           194331-31-2, DNA (human
cadherin FIB3 cDNA)
                     194382-34-8
                                  194514-50-6
                                                194516-36-4
194826-39-6, DNA (human cell line MeWo cDNA)
                                             194882-73-0
                                                           194957-26-1,
GenBank U78166
                195582-42-4
                              195651-25-3, DNA (human clone TEB4 TEB4
protein cDNA)
               195770-46-8, DNA (human clone GS1-244B22 )
196384-20-0
            196384-50-6, GenBank Y10505
                                          196384-57-3
                                                         196384-59-5
197062-81-0
             197064-41-8
                           197064-75-8
                                         197064-84-9
                                                      197064-92-9
                                         197107-15-6
197065-38-6
             197065-40-0
                           197105-43-4
                                                       197116-07-7
                          197418-46-5
197117-42-3
             197119-22-5
                                       197420-89-6
                                                       197420-97-6
197421-57-1
             197426-28-1 197428-92-5
                                         197429-69-9
                                                       197429-78-0
197465-46-6
             197465-76-2
                          198385-63-6
                                         198387-76-7
                                                       198389-31-0
                           198391-78-5
198389-88-7
             198389-97-8
                                         198393-92-9
                                                       198394-41-1
                                         252785-70-9
             198395-96-9
                           252698-52-5
                                                       252787-88-5
198394-66-0
252792-10-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
   (nucleotide sequence; expressed gene sets as markers for specific
   tumors)
252798-44-0, DNA (human gene N-CAM cDNA)
                                          252799-34-1, GenBank S73149
252800-23-0 252804-47-0 252807-38-8, GenBank S76978
                                                       252809-30-6,
GenBank S77393
                252809-85-1, GenBank S77582
                                             252813-68-6, DNA (human
gene 5-HT2A R)
                252813-97-1, DNA (human gene CD4 receptor cDNA)
252816-30-1, DNA (human fatty acid synthase cDNA) 252817-22-4, DNA
(human gene CHN cDNA)
                      252817-43-9, DNA (human gene DCC cDNA)
252818-18-1, GenBank S81083
                             252818-19-2, DNA (human gene Hs-TBX2 cDNA)
252818-28-3, GenBank S81893
                             252818-32-9, GenBank S81578
                                                          252818-62-5,
DNA (human phosphoglycerate kinase cDNA) 252820-17-0
252822-86-9, DNA (human caldecrin precursor)
                                            252823-76-0, DNA (human
gene PRB2)
           382735-60-6, DNA (human gene FSHB) 382735-91-3, DNA (human
clone pKH18 cDNA)
                   382736-10-9, DNA (human gene REN)
                                                       382757-02-0, DNA
(human gene IGHA1)
                   382866-08-2, DNA (human cell line YUSITI cDNA)
383273-66-3, DNA (human gene flt cDNA)
                                        383790-50-9, GenBank S83366
             384414-08-8 384414-72-6, GenBank M22430
384413-62-1
                                                         384417-34-9
             384419-37-8, DNA (human clone pLJ587 & pLJ663 cDNA)
384417-37-2
             384422-15-5, DNA (human annexin II cDNA plus flanks)
384419-97-0
384422-32-6, DNA (human gene VCAM1 cDNA)
                                        384423-54-5
                                                      384426-75-9
384427-24-1 384429-16-7 384430-09-5
                                         384430-35-7
                                                       384431-41-8, DNA
(human coagulation factor X gene)
                                               384435-50-1, DNA (human
                                  384433-32-3
                384436-07-1, DNA (human gene PGM1 cDNA)
gene YY1 cDNA)
                                                        384437-16-5,
                              384439-21-8 384439-27-4, DNA (human
GenBank M85165
                384438-97-5
cytochrome P-450 cDNA)
                       384439-32-1 384439-34-3, DNA (human clone pheA4
ans pheA12 cDNA)
                  384439-65-0, DNA (human gene IFNA plus flanks)
384439-70-7, GenBank M27533 384439-94-5 384439-99-0 384440-01-1
384440-03-3, DNA (human clone P-hL1-15B cDNA) 384440-22-6
                                                            384440-29-3,
DNA (human cell line U937 cDNA) 384440-42-0, DNA (human cell line LNCaP
       384440-56-6 384440-77-1, DNA (human gene VIP cDNA)
384442-83-5, GenBank X54457 384442-87-9
                                          384443-06-5, DNA (human gene
```

384443-41-8, DNA (human clone P1622 cDNA) 384444-54-6, DNA (human gene AK3) 384445-69-6 384447-91-0 384448-74-2 384449-09-6 384450-64-0 384450-79-7 384450-88-8 384451-01-8 384451-22-3, DNA (human gene CTLA4) 384451-31-4 384451-57-4, DNA (human gene LAMB2 exon 28) 384451-81-4, DNA (human gene MYL2) 384451-96-1, DNA (human gene ITGA2B cDNA) 384452-69-1, DNA (human cell line HEC cDNA) 384453-63-8, DNA (human gene c-fos) 384453-90-1, DNA (human cell line MOLT-4 cDNA) 384454-04-0, GenBank X16666 384454-72-2, 384455-61-2, DNA (human cystain S cDNA) DNA (human gene HK1 cDNA) 384457-05-0, DNA (human gene HOX4D) 384455-81-6 384456-95-5 384457-48-1, DNA (human clone Zn133, Zn102 cDNA) 384458-64-4 384459-95-4, GenBank M33493 384461-61-4, DNA (human clone ADH4:1 & ADH4:2) 384463-34-7, DNA (human cDNA) 384463-43-8, DNA (human strain cell line MKN-7 cDNA) 384463-49-4, DNA (human gene F5 cDNA) 384463-51-8 384463-53-0, DNA (human integrin α 5 cDNA) 384463-64-3, DNA (human) 384463-65-4, DNA (human clone pHGST-pi gene 384464-04-4, DNA (human gene PGY1 plus flanks) 384464-19-1 384464-25-9, DNA (human clone 2.72 cDNA) 384465-73-0 384465-75-2 384467-61-2, DNA (human gene LAMB1 cDNA) 384471-52-7, DNA (human gene 384471-82-3, DNA (human gene TMOD cDNA) 384473-92-1 GCK cDNA) 384474-61-7, DNA (human gene UOBP) 384474-63-9 384475-32-5, GenBank 384476-79-3, DNA (human neurokinin-3 384476-29-3 384476-40-8 receptor cDNA) 384478-07-3, DNA (human isolate p5aA gene ACTN1 384479-92-9, DNA (human cell line ags) 384479-94-1 384481-30-5, DNA (human gene GATA-2 cDNA) 384481-48-5, DNA 384480-46-0 (human clone Cosmid TV1) 384483-16-3, DNA (human gene casK cDNA) 384483-98-1, DNA (human C protein cDNA) 384484-53-1, DNA (human clone pHH24, pHH15B9 cDNA) 384486-06-0 384487-17-6 384492-73-3 384492-82-4 384493-06-5 384493-08-7 384493-55-4 384494-76-2, DNA (human PC1/PC3) 384496-67-7 384499-19-8 384499-60-9 384504-03-4, DNA (human keratin 13 cDNA plus flanks) 384504-50-1 384506-42-7, DNA (human elafin gene plus flanks) 384508-17-2 384512-40-7, DNA (human clone G9a-4C7 cDNA) 384513-93-3 384514-02-7 384514-61-8, DNA (human zeta-crystallin cDNA) 384515-21-3, DNA (human isolate DKB) 384515-94-0, DNA (human gene pilot cDNA) 384515-96-2 384515-98-4 384517-75-3, DNA (human nucleotide binding protein 384517-86-6 384519-06-6, DNA (human gene XPAC cDNA) 384519-36-2, DNA (human cell line KG-1 cDNA) 384519-38-4 384520-60-9 384522-51-4, DNA (human strain Cytokeratin 17) 384524-37-2, DNA (human gene SHMT2 384528-22-7, DNA (human gene AF-9 cDNA) 384528-83-0 384530-13-6 384531-47-9, GenBank L19401 384531-83-3, DNA 384529-99-1 (human thrombospondin-4 cDNA) 384532-04-1, DNA (human gene CFTR) 384537-64-8, DNA (human gene COL18A1 cDNA) 384540-86-7 384543-55-9 384548-32-7, DNA (human gene HGMP07E) 384551-83-1, DNA (human gene p130) 384552-67-4 384553-31-5 384554-99-8, DNA (human cell line KG-1 cDNA) 384555-01-5, DNA (human cell line KG-1 cDNA) 384555-10-6, DNA (human cell line HL-60 cDNA) 384555-26-4 384556-91-6 384556-98-3 384556-99-4 384557-77-1 384558-00-3, GenBank X73029 384559-61-9 384560-32-1, DNA (human glucose-6-phosphatase cDNA) 384563-19-3, DNA (human PACAP receptor cDNA) 384565-37-1 384566-95-4 384567-23-1, GenBank X71135 384571-58-8, DNA (human cell line Caco-2 384578-62-5, DNA (human cell line KG-1 cDNA) 384572-58-1 384579-90-2 384583-49-7, DNA (human clone K1) 384583-79-3 384585-25-5 384585-50-6, DNA (human clone hek1, hek3, hek5 384584-68-3 384586-34-9 384586-53-2 384587-02-4, DNA (human clone h20B1) 384587-72-8, DNA (human clone LUCA-1 cDNA) 384588-08-3, DNA (human isolate patient MZ2) 384588-16-3, DNA (human isolate patient MZ2) 384588-39-0 384589-23-5 384589-73-5, DNA (human cell line keratinocytes cDNA) 384591-52-0 384592-16-9, DNA (human gene hOC-2 384593-14-0 384593-83-3, DNA (human gene GPR1) 384599-49-9 cDNA)

384608-09-7, DNA (human gene FUT2)

384612-83-3, DNA (human gene TRADD cDNA)

384602-52-2

384612-79-7

384608-55-3

384614-14-6

```
384619-85-6, DNA (human clone apM1 cDNA)
                                             384619-95-8
                                                            384620-48-8, DNA
     (human PRK2 cDNA)
                        384620-80-8
                                     384621-38-9, DNA (human cell line
    MZ2-MEL.43 cDNA)
                       384626-89-5
                                    384627-00-3
                                                 384627-10-5, DNA (human
    clone S171 cDNA)
                       384631-27-0 384631-30-5, DNA (human clone F-T03796
            384631-48-5, DNA (human cell line KG-1 cDNA)
                                                          384633-60-7
                  384640-82-8
                               384647-11-4
                                            384648-77-5, DNA (human cell
    384640-80-6
                         384649-87-0, DNA (human gene NPM-MLF1 cDNA)
    line LB33-MEL.A-1 )
    384650-74-2, DNA (human gene mat1 cDNA)
                                            384653-03-6
                                                          384653-31-0
    384653-54-7
                  384653-65-0
    RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (nucleotide sequence; expressed gene sets as markers for specific
       tumors)
IT
    384655-21-4, DNA (human gene MIHB cDNA)
                                             384655-55-4
                                                           384655-92-9, DNA
                             384657-76-5 384657-95-8 384662-97-9, DNA
     (human gene PDE1A cDNA)
                              384664-52-2, DNA (human gene FRDA)
     (human mammaglobin cDNA)
                  384667-57-6, GenBank U50822
    384664-90-8
                                              384681-06-5
                                                             384681-35-0
    384683-28-7, DNA (human PRSM1 cDNA) 384686-54-8
                                                      384689-33-2
    384690-93-1, DNA (human p38Beta MAP kinase cDNA) 384691-45-6
    384691-51-4, DNA (human cell line LNCaP cDNA) 384693-02-1, DNA (human
    cell line KG-1 cDNA)
                          384693-58-7, DNA (human gene TCTEL1 cDNA)
    384695-06-1
                  384695-13-0, DNA (human clone 27G4 cDNA) 384695-15-2, DNA
     (human gene CMKBR5) 384695-17-4, DNA (human cell line HaCaT cDNA)
    384696-51-9
                  384698-02-6, DNA (human gene GPR19) 384726-43-6, DNA
     (human gene bbc6 cDNA)
                            384726-68-5, DNA (human hGATA-6 cDNA)
    384728-11-4 384728-15-8 384728-56-7 384729-16-2 384731-22-0,
                    384733-15-7 384735-58-4 384746-66-1, DNA (human
    GenBank D84290
    gravin)
              384747-60-8 384748-30-5 384748-92-9
                                                       384749-88-6, DNA
     (human clone H361 cDNA) 384750-18-9, DNA (human gene hTcf-4 cDNA)
    384750-36-1
                  384762-33-8 384763-37-5, DNA (human gene hsReq)
    384765-62-2, DNA (human clone hg00111s1 cDNA)
                                                  384765-71-3, DNA (human
    clone HG1015 cDNA)
                       384766-18-1, DNA (human 15S-lipoxygenase cDNA)
                              384779-95-7, DNA (human clone GS3340 cDNA)
    384767-18-4
                  384770-11-0
                  384976-11-8, DNA (human clone 1292. cDNA)
    384780-42-1
                                                           384976-21-0
                  384976-60-7, DNA (human gene H-plk cDNA)
    384976-57-2
                                                            384976-62-9, DNA
     (human gene IFNAR cDNA) 384976-87-8, DNA (human cell line HL60 clone c5
        384976-91-4, DNA (human clone 4X.3 ) 384977-16-6, DNA (human gene
    TRY1 cDNA)
                 384977-21-3 384977-23-5, DNA (human gene B12 cDNA)
    384977-30-4
                  384977-66-6
                              384977-70-2 384978-09-0, DNA (human gene MUT
           384979-34-4
                        384983-76-0
                                       384986-45-2
                                                    384997-12-0
    384997-93-7, DNA (human carboxypeptidase a cDNA) 384998-64-5
                  385027-38-3, DNA (human gene ASP cDNA)
    385011-13-2
                                                          385027-63-4
    385028-04-6
                               385038-39-1 385042-35-3
                  385032-56-4
                                                         385043-25-4
    385043-57-2
                  385052-66-4, DNA (human acyl-CoA dehydrogenase cDNA)
    385074-83-9, DNA (human gene DTK cDNA) 385079-81-2 385081-26-5, DNA
    (human gene PCOLCE cDNA) 385082-06-4, DNA (human clone FL-2 cDNA)
    385086-18-0, DNA (human gene CD39 cDNA) 385089-95-2, DNA (human clone
    HHH4 gene IHH cDNA) 385090-26-6, DNA (human clone hKvBeta3 cDNA)
    385091-52-1, DNA (human clone phPCaR-5.2 cDNA) 385092-31-9 385093-03-8
                385097-61-0 385100-02-7 385101-13-3, DNA (human BA46
    385093-04-9
            385101-77-9, DNA (human E2F-5 cDNA) 385101-84-8, DNA (human
    clone RA337M, GS4642 cDNA) 385102-06-7, DNA (human CLPP cDNA)
    385105-64-6 385106-71-8, DNA (human clone SB2 cDNA) 386563-36-6,
    GenBank S77415
                     389173-70-0 389174-60-1 389175-19-3, DNA (human gene
            389176-63-0, DNA (human cell line A431 cDNA)
                                                          389179-81-1
                  389179-85-5 389179-86-6 389179-90-2
    389179-82-2
                                                           389179-95-7, DNA
    (human gene COL5A2) 389180-03-4 389180-06-7, GenBank X05345
    389180-07-8, DNA (human gene HPX) 389180-28-3, GenBank J05252
```

```
389180-41-0
             389180-49-8
                           389180-50-1 389180-95-4, DNA (human gene
MAOA cDNA)
            389181-47-9, DNA (human clone cos TCFP-HPV-3) 389181-48-0,
DNA (human gene SAP-1 cDNA)
                             389181-81-1, GenBank X03350
                                                          389181-84-4
389181-86-6, DNA (human clone HL-14 cDNA)
                                          389181-87-7
                                                       389181-95-7, DNA
(human gene C1R cDNA)
                       389181-98-0
                                   389182-00-7, DNA (human CENP-B cDNA)
389182-03-0
             389182-21-2, DNA (human 1207-amino acid protein
       389182-22-3
                     389182-31-4
                                  389182-39-2, GenBank M34309
389182-46-1 389182-62-1, GenBank M26041
                                          389182-65-4
                                                        389182-73-4
389182-88-1, GenBank M13231
                            389182-90-5
                                          389182-94-9
                                                        389182-95-0,
                389182-98-3, DNA (human cell line HT29 cDNA)
GenBank M11749
389183-42-0, DNA (human gene HPF2 cDNA)
                                        389183-54-4, DNA (human clone
pSK-hB(c1) cDNA)
                389183-57-7, DNA (human gene AHCY cDNA) 389183-59-9,
DNA (human gene CTSD plus flanks) 389183-86-2
                                                389183-99-7, DNA (human
clone CD8-beta.1 cDNA) 389184-02-5, DNA (human clone F225 cDNA)
389184-04-7, GenBank Y07512
                            389184-05-8 389184-15-0
                                                        389184-28-5, DNA
(human gene HOX3D) 389184-39-8, DNA (human gene CD59) 389184-61-6, DNA
(human clone HACTSG-112 ) 389184-63-8 389184-64-9
                                                     389184-65-0, DNA
(human clone pHAIVG[5.1,5.2])
                               389184-66-1
                                             389184-73-0, DNA (human
            389184-77-4, DNA (human gene C7 cDNA)
gene HEXA)
                                                  389184-84-3, DNA
(human gene CYB5 cytochrome b5 cDNA) 389184-87-6, DNA (human gene CST3)
389184-90-1 389184-94-5, DNA (human gene FGB cDNA)
                                                    389185-20-0
389185-25-5, DNA (human clone pHMCH2 cDNA) 389185-38-0, DNA (human gene
      389185-40-4, DNA (human cell line HPAF-CD11 cDNA)
                                                         389185-43-7,
DNA (human gene PDGFA) 389185-55-1 389185-66-4 389185-72-2
389186-21-4, DNA (human cell line GM3299; GM637 cDNA)
                                                     389186-38-3, DNA
(human clone 5.1, 9.2, 9J cDNA) 389186-51-0 389186-69-0, DNA (human
clone D1 cDNA) 389186-93-0, DNA (human gene CGB cDNA)
                                                        389189-06-4, DNA
(human gene APOA1 plus gene APOC3)
                                   389189-13-3
                                                389189-14-4
389189-17-7
            389189-18-8, DNA (human gene F8C cDNA)
                                     389189-26-8
389189-25-7, DNA (human gene CTLA1)
                                                  389189-60-0, GenBank
       389189-61-1, GenBank M31013
                                    389189-65-5 389189-69-9, DNA
(human gene reg plus flanks)
                            389189-81-5, DNA (human gene TGFB1 cDNA)
389189-82-6, DNA (human gene uPA plus flanks) 389189-83-7, DNA (human
                       389190-55-0, DNA (human gene VCAM1)
          389190-15-2
gene VDR)
389190-70-9, DNA (human clone ccglp cDNA) 389190-72-1, DNA (human cyclin
       389190-74-3, DNA (human gene LGALS2) 389190-79-8, DNA (human
cystatin S cDNA plus flanks) 389190-97-0, DNA (human gene DMD cDNA)
389191-21-3, DNA (human gene EDN1)
                                  389191-82-6 389191-93-9
389192-40-9, DNA (human pyruvate kinase gene) 389192-44-3
389192-47-6, DNA (human gene cysteine-richprotein) 389192-77-2
             389195-95-3, DNA (human gene GSTM5 cDNA)
389193-51-5
                                                       389196-47-8
             389200-11-7, DNA (human clone CENPE cDNA)
                                                      389200-16-2,
389200-09-3
GenBank X02875
                389200-44-6 389200-61-7, DNA (human receptor
         389200-80-0
                       389202-86-2, DNA (human cell line CRL-1262 cDNA)
TR3 cDNA)
389203-61-6, DNA (human clone pP1-3, pP1-8 cDNA) 389203-74-1
389204-43-7 389204-60-8, DNA (human clone RES4-4 cDNA)
                                                         389205-56-5,
DNA (human gene GLUR5 cDNA) 389206-66-0
                                          389208-34-8
                                                        389209-27-2, DNA
(human gene X104 cDNA) 389210-70-2 389210-89-3 389212-46-8
389214-42-0, DNA (human clone HRGR1-2 cDNA)
                                            389217-81-6
                                                          389217-93-0,
DNA (human unknown cDNA) 389220-22-8 389231-42-9, DNA (human clone
cosmid 4.10 ) 389233-90-3 389234-19-9 389234-77-9 389234-85-9
                                           389243-20-3, DNA (human clone
389243-13-4, DNA (human clone HPEPT1 cDNA)
14 cDNA)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
   (nucleotide sequence; expressed gene sets as markers for specific
   tumors)
389259-07-8
             389261-10-3
                           389278-87-9, DNA (human Snf2-b gene cDNA plus
flanks) 389278-90-4, DNA (human clone S240ii117/zap112 cDNA)
389283-46-9, GenBank U33202 389283-47-0 389297-61-4, DNA (human clone
```

```
389308-01-4, DNA (human isolate Germany cDNA)
ph3b7 )
          389299-59-6
389310-50-3
             389311-33-5 389316-25-0, DNA (human gene SSAT plus flanks)
389316-69-2, DNA (human clone hVH-5 cDNA)
                                          389317-49-1, DNA (human clone
                  389322-16-1, DNA (human clone x61 cDNA)
HPG Ca 5.1 cDNA)
                                                         389322-17-2
                          389331-49-1, DNA (human gene CCK-A)
389323-32-4
             389330-22-7
389331-81-1
              389332-59-6, DNA (human cell line G2 cDNA)
389335-64-2, DNA (human GPR-9-6 gene)
                                     389336-58-7
                                                  389340-64-1
389341-59-7
             389342-02-3 389346-64-9 389346-96-7
                                                    389350-71-4
             389355-89-9
                         389358-75-2 389358-86-5
389355-49-1
                                                      389359-76-6
             389361-66-4 389361-87-9 389362-45-2
389361-42-6
                                                      389363-92-2
             389365-23-5 389365-91-7 389369-12-4, DNA (human cell
389364-11-8
line 5583-S cDNA)
                   389370-55-2 389371-19-1 389374-57-6 389375-30-8,
DNA (human gene ARS) 389375-84-2
                                  389376-31-2, DNA (human gene HRR-1
        389376-99-2
                     389378-60-3
                                  389382-78-9 389386-87-2, DNA (human
MAP kinase kinase MEK5b cDNA)
                             389393-68-4
389395-41-9
             389396-06-9 389398-07-6
                                        389398-09-8
                                                      389399-94-4
389400-17-3
             389405-04-3 389405-38-3 389406-79-5
                                                      389407-07-2
389408-31-5
             389409-36-3 389409-47-6 389410-70-2
                                                      389412-14-0
389416-85-7
             389422-93-9 389423-18-1 389423-40-9, DNA (human clone
             389424-20-8 389425-17-6 389428-51-7 389429-86-1, DNA
RP3-453A3 )
 (human calponin cDNA) 389430-45-9 389430-49-3
                                                389432-09-1
389435-18-1
             389440-10-2
                          389440-92-0 389443-42-9
                                                      389445-40-3
389445-50-5
             389446-70-2
                          389447-25-0
                                       389447-86-3
                                                      389448-05-9
389460-85-9
             389461-02-3 389464-31-7, DNA (human gene EXTL2 cDNA)
389464-68-0
             389464-77-1 389465-06-9 389472-07-5 389473-43-2
389473-73-8
             389473-74-9 389479-72-5 389480-33-5
                                                      389481-01-0
389481-42-9
             389481-47-4 389481-56-5 389481-59-8
                                                      389482-66-0
389484-22-4
             389485-84-1 389486-04-8 389494-80-8
                                                      389497-95-4
389498-02-6
             389499-40-5 389505-00-4 389506-23-4
                                                    389506-68-7
             389507-94-2 389509-41-5 389509-52-8, DNA (human clone
389506-96-1
MU1 cDNA) 389509-76-6 389512-70-3 389513-27-3 389514-04-9
389514-27-6
             389515-91-7
                          389515-97-3 389520-98-3
                                                    389522-61-6
389540-48-1
             389542-93-2 389543-23-1
                                        389544-47-2
                                                      389544-49-4
389547-87-9
             389547-95-9 389548-22-5 389549-01-3
                                                      389550-58-7
389551-99-9
             389552-22-1 389554-54-5 389554-67-0
                                                      389555-50-4
389555-89-9
             389556-47-2 389557-31-7 389562-01-0
                                                      389564-59-4, DNA
(human gene hCTR2 cDNA) 389695-14-1 389699-60-9 389699-75-6
389721-97-5 390187-80-1 390188-17-7, DNA (human gene ArgRS cDNA)
391523-46-9, DNA (human gene CD9 cDNA) 391524-31-5, DNA (human cell line
HT29 cDNA)
            391524-68-8, DNA (human gene PI cDNA) 391524-69-9, DNA
 (human \alpha-actin cDNA plus flanks)
                                391524-76-8 391524-78-0
391524-80-4, DNA (human gene CLG1 cDNA)
                                      391524-97-3
                                                      391524-99-5
             391525-12-5 391525-13-6 391525-15-8 391525-31-8, DNA
391525-02-3
(human gene NMOR2 cDNA) 391525-32-9 391525-34-1, DNA (human plus gene
rps24 cDNA)
            391525-35-2, GenBank M25756 391525-36-3 391525-37-4,
GenBank M19888 391525-38-5 391525-41-0 391525-60-3, DNA (human cell
line HL-60 cDNA) 391525-65-8
                              391525-71-6 391525-76-1
                                                         391525-77-2
            391525-90-9, DNA (human gene ddc cDNA)
391525-79-4
                                                     391525-91-0
391525-97-6, DNA (human gene CHMR5 gene plus flanks)
                                                     391526-01-5
             391526-32-2, GenBank M29877 391526-34-4
391526-23-1
                                                        391526-39-9
391526-47-9
             391526-51-5, DNA (human cell line W38 and U2-OS cDNA)
391526-52-6
             391526-54-8, DNA (human gene CEA cDNA)
                                                    391526-60-6
391526-62-8, GenBank X07438 391526-66-2, DNA (human gene CTSE cDNA)
391526-67-3
             391526-68-4, DNA (human gene QDPR cDNA) 391526-73-1
391526-80-0
             391526-85-5, DNA (human gene GLUD1)
                                                391526-88-8
391526-91-3
             391526-98-0 391526-99-1, DNA (human gene SCYA1)
391527-01-8, DNA (human interferon-\alpha 6 gene)
                                           391527-02-9, GenBank
        391527-13-2 391527-14-3 391527-20-1 391527-26-7
391527-29-0, DNA (human gene LYZ cDNA) 391527-30-3, DNA (human gene LYZ
      391527-35-8 391527-37-0, DNA (human gene NMOR1 cDNA)
· cDNA)
```

391527-56-3, DNA (human gelsolin cDNA plus

391527-46-1

391527-47-2

```
flanks)
            391527-57-4 391527-58-5 391527-68-7, GenBank M24486
                                                          391528-05-5
    391527-69-8
                  391527-72-3
                               391527-81-4
                                            391527-87-0
    391528-06-6
                  391528-10-2
                               391528-16-8
                                            391528-20-4, DNA (human gene FAH
            391528-22-6, DNA (human gene TRPM-2 exons 7-9)
                                                           391528-33-9
    391528-38-4
    RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (nucleotide sequence; expressed gene sets as markers for specific
       tumors)
    391528-40-8, DNA (human cell line HeLa clone F6 cDNA)
ΙT
                                                          391528-52-2
    391528-54-4 391528-68-0, DNA (human gene PMP1 cDNA)
                                                          391528-70-4, DNA
                          391528-75-9 391528-90-8, DNA (human IgG)
     (human gene p78 cDNA)
    391528-92-0, DNA (human P-cadherin cDNA plus flanks) 391529-03-6, DNA
     (human clone p-lambda-H6-7 cDNA) 391529-04-7 391529-06-9, DNA (human
    gene ACTB plus flanks) 391529-09-2, DNA (human clone pTF. gene ADRB2
                        391529-13-8, DNA (human gene CLTA cDNA)
            391529-12-7
    391529-20-7
                 391529-41-2
                               391529-46-7 391529-51-4 391529-52-5
    391529-72-9, DNA (human gene MGMT protein cDNA)
                                                    391529-91-2
    391529-96-7, DNA (human gene RBP1 cDNA)
                                           391529-99-0
                                                         391530-24-8
    391530-32-8 391530-34-0 391530-42-0
                                           391530-80-6
                                                         391530-83-9, DNA
     (human cell line Hs68 cDNA) 391530-84-0, DNA (human iron regulatory
              391530-92-0 391531-06-9, DNA (human gene DBI protein
    factor)
    cDNA)
          391531-14-9, DNA (human gene IGHG3 cDNA) 391531-19-4, GenBank
    M21054 391531-23-0, DNA (human clone lambda TI-C1 cDNA) 391531-30-9
    391531-32-1, DNA (human clone pCOX7.183 ) 391532-11-9 391532-25-5, DNA
     (human gene COL1A2 cDNA) 391532-26-6 391532-27-7 391532-29-9, DNA
     (human gene c-yes-1 protein cDNA) 391532-46-0, DNA (human
    serine protease gene) 391532-48-2 391532-53-9, DNA (human clone M1-M5
    and B1-B4 cDNA) 391532-55-1, DNA (human gene VCL protein cDNA)
    391532-66-4
                 391532-68-6
                               391532-69-7
                                            391532-74-4 391532-75-5
                                            391533-27-0, DNA (human gene
    391533-05-4
                391533-20-3 391533-21-4
             391533-29-2, DNA (human gene CTSS cDNA) 391533-31-6, DNA
    K-sam-I)
     (human desmin gene) 391533-33-8, DNA (human gene IGFBP3) 391533-36-1
    391533-50-9, DNA (human gene FMO2 cDNA) 391533-71-4 391533-80-5, DNA
    (human gene PLAT) 391533-87-2 391534-11-5 391534-13-7 391534-20-6
    391534-28-4, DNA (human mevalonate kinase cDNA) 391534-43-3
    391534-46-6 391534-62-6 391534-72-8 391534-87-5, DNA (human serum
    protein cDNA) 391534-93-3, DNA (human gene MK)
                                                   391534-95-5,
    DNA (human clone C328-10 cDNA) 391535-13-0, DNA (human cell line T47D
            391535-29-8 391535-52-7 391535-66-3 391535-84-5
    391535-88-9
                 391536-06-4, DNA (human cell line BJA cDNA)
                                                            391536-08-6
    391536-09-7, DNA (human cell line B5/589 cDNA) 391536-12-2, DNA (human
    gene MYL5 cDNA)
                     391536-19-9, DNA (human transcription activator cDNA)
    391536-20-2, DNA (human gene TLE1 cDNA) 391536-22-4 391536-35-9
    391536-65-5, DNA (human immunophilin cDNA) 391536-66-6
                                                            391536-67-7,
    DNA (human gene PLOD cDNA) 391536-73-5, DNA (human gene RPL37A cDNA)
    391537-03-4, DNA (human gene NPYY1 cDNA) 391537-19-2 391537-21-6
                  391537-47-6 391537-48-7 391538-38-8
    391537-41-0
                                                          391538-40-2
                  391538-55-9
                              391538-96-8 391538-98-0
    391538-41-3
                                                          391539-19-8
    391539-22-3
                  391539-25-6, DNA (human cell line Hela clone HL-27 )
    391539-32-5
                  391539-44-9 391539-59-6 391539-63-2 391539-74-5, DNA
     (human cell line KB cell line cDNA) 391539-84-7 391539-90-5, DNA
     (human cell line KG-1 cDNA) 391539-94-9, DNA (human cell line KG-1 cDNA)
    391540-03-7
                391540-05-9, DNA (human cell line KG-1 cDNA) 391540-08-2,
    DNA (human cell line KG-1 cDNA) 391540-09-3, DNA (human cell line KG-1
            391540-13-9, DNA (human cell line KG-1 cDNA) 391540-14-0, DNA
    (human cell line KG-1 cDNA) 391540-35-5 391540-39-9 391540-52-6
    391540-55-9 391540-62-8 391540-73-1, DNA (human Mel-18 protein
          391540-89-9, DNA (human protocadherin 42 cDNA) 391541-10-9, DNA
    cDNA)
```

```
(human gene GRK5 cDNA)
                        391541-27-8 391541-33-6
                                                    391541-38-1, DNA
(human cell line THP-1 cDNA) 391541-39-2 391541-65-4 391541-70-1
391541-71-2, DNA (human cell line HeLa S3 cDNA)
                                                391541-80-3, DNA (human
                 391541-96-1 391542-02-2, DNA (human gene PPP3CA cDNA)
gene CAST cDNA)
391542-07-7 391542-12-4, DNA (human cell line Namalva CDNA)
391542-21-5, DNA (human clone S100D cDNA) 391542-28-2, DNA (human
kinesin light chain cDNA) 391542-40-8, DNA (human gene MIF)
391542-58-8, DNA (human clone pKOT158 cDNA) 391542-60-2, DNA (human
fibrillin cDNA)
                 391542-61-3
                               391542-96-4, DNA (human surfactant
protein A cDNA)
                 391542-98-6, DNA (human gene GPI-H cDNA)
391543-01-4
             391543-06-9
                           391543-17-2, DNA (human gene ADORA1 cDNA)
391543-62-7
             391543-76-3
                           391543-79-6 391543-86-5, DNA (human gene
DAG1 cDNA)
            391543-95-6, DNA (human A2b adenosine receptor
cDNA)
        391544-00-6
                     391544-09-5
                                   391544-19-7
                                                 391544-21-1, DNA (human
I-plastin cDNA)
                 391544-24-4
                              391544-30-2
                                             391544-39-1
                                                           391544-42-6
391544-47-1
             391544-59-5 391544-70-0
                                        391544-74-4, DNA (human cell
line HeLa cells )
                   391544-80-2, DNA (human clone pHPM11 cDNA)
391544-83-5
             391544-90-4, DNA (human prolylcarboxypeptidase cDNA)
391545-00-9
              391545-03-2
                           391545-12-3
                                        391545-13-4
                                                       391545-15-6
             391545-18-9
                           391545-20-3
                                        391545-23-6
                                                       391545-41-8, DNA
391545-16-7
(human gene MC5R)
                   391545-44-1, DNA (human cell line KG-1 cDNA)
             391545-46-3, DNA (human cell line KG-1 cDNA)
391545-45-2
                                                            391545-47-4,
DNA (human clone PO2ST9 cDNA)
                              391545-58-7, DNA (human cell line KG-1
        391545-62-3
                     391545-64-5, DNA (human 5T4 oncofetal antigen)
              391545-67-8, DNA (human cell line KG-1 cDNA)
391545-65-6
                                                            391545-96-3
391545-97-4
              391546-08-0, DNA (human protein kinase C
          391546-20-6, DNA (human cell line HL60 cDNA)
                                                         391546-29-5, DNA
(human caltractin cDNA) 391546-48-8, GenBank L25880 391546-58-0
391546-63-7, DNA (human cell line Molt4 cDNA)
                                               391546-64-8, DNA (human
histidase cDNA)
                 391546-77-3 391546-78-4 391546-79-5, DNA (human gene
EHHADH cDNA)
              391546-82-0
                            391546-86-4
                                          391546-87-5, DNA (human Na+
channel protein cDNA)
                       391546-90-0, DNA (human cell line KG-1
                     391546-98-8
                                  391547-09-4, DNA (human gene garp
cDNA)
        391546-94-4
cDNA)
        391547-50-5
                     391547-51-6, DNA (human 56K autoantigen cDNA)
             391547-70-9, DNA (human BST-2 cDNA)
                                                   391547-83-4, DNA
(human clone Lambda GS2-1 cDNA) 391547-88-9, DNA (human clone 2004-1407
                 391548-04-2, DNA (human gene ARL3 cDNA)
    391547-92-5
                                                           391548-10-0
             391548-27-9
                          391548-28-0, DNA (human cell line KATO-III
391548-22-4
        391548-59-7
                     391548-61-1
                                  391548-89-3, DNA (human gene CAT cDNA)
391549-05-6, GenBank X69920
                              391549-19-2, DNA (human isolate Japanese
        391549-25-0 391549-33-0
                                   391549-55-6, GenBank D29675
391549-62-5, DNA (human cell line KG-1 cDNA)
                                            391549-78-3, DNA (human
                            391549-81-8, DNA (human gene NNMT cDNA)
cell line Raji DAD-1 cDNA)
391549-83-0, DNA (human ORF cDNA)
                                   391549-87-4
                                                 391549-91-0
391549-96-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
   (nucleotide sequence; expressed gene sets as markers for specific
   tumors)
391550-24-6
              391550-26-8
                           391550-27-9
                                         391550-28-0, DNA (human cell
                  391550-29-1, DNA (human cell line KG-1 cDNA)
line KG-1 cDNA)
              391550-44-0, DNA (human gene mig-2 plus 3'-flank)
391550-40-6
391550-50-8
              391550-54-2, DNA (human cell line KG-1 cDNA)
                                                            391550-59-7,
DNA (human GP36b glycoprotein cDNA)
                                     391550-73-5
                                                   391550-75-7
              391551-07-8, DNA (human clone clone 270-4 cDNA)
391551-01-2
              391551-43-2, DNA (human cell line Hela S3 cDNA)
391551-36-3
                           391551-91-0, DNA (human oviductal glycoprotein
              391551-56-7
        391552-21-9, DNA (human gene Eps8 cDNA)
                                                391552-25-3
391552-27-5, DNA (human Csa-19 cDNA) 391552-40-2
                                                   391553-02-9
             391553-58-5
                          391553-66-5 391553-67-6, DNA (human gene
391553-41-6
```

TΤ

HEK8 cDNA) 391553-75-6, DNA (human cdc27 gene) 391553-79-0 391553-88-1, DNA (human myosin-IC) 391554-14-6, DNA (human clone MN1 391554-19-1 391554-21-5, DNA (human gene BNIP3 cDNA) 391554-24-8 391554-27-1, DNA (human cell line KG-1 cDNA) 391554-32-8, DNA (human cell line KG-1 cDNA) 391554-37-3, DNA (human cell line KG-1 391554-44-2, DNA (human cell line COLO 205 cDNA) 391554-91-9 391555-10-5, DNA (human gene CRALBP) 391555-28-5, DNA (human clone pKOT161 cDNA) 391555-29-6 391555-44-5 391555-46-7, DNA (human cell line KG-1 cDNA) 391555-48-9 391555-49-0, DNA (human cell line KG-1 cDNA) 391555-51-4, DNA (human cell line KG-1 391555-54-7, DNA (human cell line KG-1 cDNA) 391555-55-8, DNA (human clone pcDNA.HS.2 cDNA) 391556-64-2 391556-66-4, DNA (human 391556-73-3, DNA (human clone pG77-12 cDNA) clone Lutheran) 391556-78-8, DNA (human gene TROP-2) 391556-81-3 391556-87-9 391556-92-6, DNA (human gene ANK-3 cDNA) 391556-93-7 391556-94-8, DNA (human clone G to O cDNA) 391557-06-5, DNA (human initiation factor 2 391557-07-6 391557-48-5, DNA (human SURF-1 cDNA) 391557-52-1 391557-62-3, DNA (human gene E2F-4 cDNA) 391557-77-0 391557-91-8, DNA (human gene CPT1) 391560-53-5 391560-56-8 391560-64-8, DNA (human 391560-81-9, GenBank X82279 391562-13-3 clone hTq737 cDNA) 391564-21-9, DNA (human clone 3-5 & 7-1) 391564-47-9, DNA (human paxillin cDNA) 391565-14-3 391566-19-1 391566-25-9 391568-60-8, DNA (human gene CYP51) 391569-13-4 391569-19-0, DNA (human gene MORT1 391569-86-1, DNA (human clone pHSMP6 SMP-30 cDNA) 391570-28-8 391570-76-6 391571-54-3 391571-60-1, DNA (human clone B1-T1 cDNA) 391576-13-9, DNA (human casein kinase I-epsilon 391575-76-1 391576-47-9 391581-29-6 391581-46-7 391581-52-5 391581-56-9, DNA (human prostasin cDNA plus flanks) 391581-63-8, DNA (human clone apM2 cDNA) 391583-63-4 391584-78-4, DNA (human gene TBX2 391584-82-0 391584-83-1 391584-97-7, DNA (human 391584-79-5 gene HMGI-C) 391584-98-8, DNA (human blood gene DARC plus flanks) 391588-46-8, DNA (human gene ST13 cDNA) 391588-47-9 391588-59-3, DNA (human clone s153 cDNA) 391588-65-1, DNA (human gene Nramp2 cDNA) 391588-67-3, DNA (human clone S31i125 cDNA) 391590-87-7, DNA (human cell line C-Li21 cDNA) 391590-88-8, GenBank U29463 391590-98-0, DNA (human CAS cDNA) 391591-07-4 391591-14-3 391591-31-4 391591-35-8, DNA (human cell line MKN28 cDNA) 391591-66-5 391591-67-6 391592-22-6, DNA (human clone pBO52 cDNA) 391758-89-7, DNA (human clone pHTO3 cDNA) 391759-27-6 391759-28-7 391759-38-9 391759-88-9, DNA (human gene 391763-22-7 391763-24-9, DNA (human gene CYP2A13) SCNN1B cDNA) 391763-33-0, DNA (human gene hsRPB8) 391763-34-1 391763-44-3, DNA (human clone GT247 cDNA) 391763-46-5 391763-54-5 391765-26-7 391765-33-6, DNA (human clone 108448 cDNA) 391765-35-8 391765-30-3 391766-15-7, DNA (human gene SCCA2 cDNA) 391766-16-8 391766-17-9, DNA (human gene orf cDNA) 391767-79-6 391767-84-3 391768-57-3 391769-35-0 391770-17-5 391770-18-6, DNA (human cell line SKBR-3 cDNA) 391770-73-3 391770-28-8 391770-95-9 391771-45-2 391772-31-9 391772-37-5, DNA (human cell line KG-1 cDNA) 391772-40-0, DNA (human 391772-42-2, DNA (human cell line KG-1 cDNA) cell line KG-1 cDNA) 391772-44-4 391772-48-8 391772-51-3, DNA (human cell 391772-43-3 line KG-1 cDNA) 391772-53-5, DNA (human cell line KG-1 cDNA) 391772-55-7, DNA (human gene DNM cDNA) 391772-68-2 391772-74-0 391772-75-1, DNA (human cell line KG-1 cDNA) 391772-78-4, DNA (human cell line KG-1 cDNA) 391772-82-0, DNA (human cell line KG-1 cDNA) 391772-84-2, DNA (human cell line KG-1 cDNA) 391772-90-0 391772-94-4 391773-74-3 391773-95-8, DNA (human gene creb-rp cDNA) 391774-02-0, DNA (human gene UBCH5B cDNA) 391774-05-3 391774-06-4 391774-10-0 391774-60-0, GenBank U40990 391775-25-0, DNA (human gene CTF1 cDNA) 391775-31-8, GenBank X91196 391775-77-2 391775-83-0 391775-84-1, DNA (human clone A111; A85) 391776-15-1, DNA (human gene acidic calponin

```
391776-51-5
                     391777-01-8 391777-02-9
                                              391777-17-6
391779-93-4
             391780-95-3 391780-97-5 391781-88-7 391781-96-7, DNA
(human gene DSS1 protein cDNA)
                              391782-07-3 391782-13-1
391782-24-4
             391782-26-6 391782-31-3 391782-32-4, GenBank Z49826
391783-00-9
             391783-13-4, DNA (human dynamitin cDNA) 391783-87-2, DNA
(human gene htMART cDNA) 391783-94-1 391784-77-3, DNA (human gene MPD
              391784-82-0, DNA (human glutathione synthetase
protein cDNA)
      391785-32-3, DNA (human gene OC-116KDa cDNA) 391785-36-7, DNA
(human gene six1 cDNA) 391785-95-8 391785-96-9, DNA (human clone MB4)
391785-98-1, DNA (human gene CRISP-3 protein cDNA)
391787-70-5, DNA (human protein XMP cDNA plus flanks)
391787-72-7 391787-73-8 391787-88-5, DNA (human clone SFA-1 cDNA)
391788-30-0, DNA (human gene Diff33 cDNA)
                                         391788-48-0 391788-68-4
391789-78-9 391789-81-4, DNA (human cell line OsA-Cl cDNA)
                                                            391790-49-1
391791-22-3, DNA (human ryudocan core protein gene)
391791-70-1, DNA (human gene Grb14 cDNA) 391791-87-0, DNA (human gene
NKCC2 cDNA) 391791-88-1, DNA (human cell line HeLa cell cDNA)
391792-14-6, GenBank L77563 391792-21-5 391793-92-3 391794-37-9
391794-65-3 391794-68-6 391794-94-8 391794-96-0, DNA (human gene
      391795-85-0, DNA (human Smad1 cDNA) 391795-87-2
pyst2)
                                                        391796-80-8
391797-11-8 391797-13-0 391797-26-5 391797-54-9, DNA (human clone
KEalpha4.2 cDNA) 391797-58-3, DNA (human clone KBbeta3.2 cDNA)
391797-69-6, GenBank U35005 391798-12-2, DNA (human AEBP1 cDNA)
391798-13-3
            391798-43-9, DNA (human gene HLA-H cDNA) 391798-44-0, DNA
(human clone tob4 cDNA)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
   (nucleotide sequence; expressed gene sets as markers for specific
   tumors)
                                        391800-73-0
391799-41-0, DNA (human gene PP2A cDNA)
                                                     391800-83-2
391800-94-5 391801-55-1 391803-82-0
                                      391803-84-2
                                                     391803-95-5
391803-97-7, DNA (human cell line KG-1 cDNA) 391804-00-5, DNA (human
cell line KG-1 cDNA) 391804-01-6 391804-02-7
                                                391804-89-0
391804-94-7 391806-14-7, DNA (human gene MAGE9) 391806-64-7, DNA
(human gene LPP cDNA) 391807-29-7, DNA (human gene XPF cDNA)
391807-30-0, DNA (human neutral calponin cDNA) 391807-54-8, DNA (human
                391807-57-1 391808-42-7 391808-51-8 391809-32-8,
clone D3A cDNA)
DNA (human cell line P39 cDNA) 391809-38-4, DNA (human gene hMAD-3)
391809-79-3 391810-13-2 391810-62-1, DNA (human synapsin IIb cDNA)
391810-68-7, DNA (human clone 15B cDNA) 391810-69-8 391811-19-1, DNA
(human gene RBP56 cDNA) 391811-20-4 391811-23-7, DNA (human clone
cos43 ) 391811-32-8 391811-33-9, DNA (human gene hBD-1 cDNA)
391811-46-4 391811-47-5 391811-60-2
                                       391811-64-6, DNA (human gene
hBRAVO/Nr-CAM)
              391811-72-6, DNA (human neogenin cDNA) 391812-49-0
391812-61-6 391812-63-8 391813-81-3 391814-44-1 391814-45-2
391814-60-1
             391814-64-5, DNA (human gastricsin cDNA)
                                                    391814-66-7, DNA
(human clone DAZ-e11 cDNA) 391814-99-6 391815-01-3 391815-08-0
391815-14-8 391815-16-0, DNA (human clone HA6690 cDNA) 391815-18-2
            391815-49-9 391815-86-4 391815-90-0, DNA (human gene C3f
391815-20-6
      391815-92-2 391816-23-2 391816-49-2 391817-74-6
cDNA)
391818-97-6 391819-61-7 391819-85-5 391819-88-8, DNA (human p0071
protein cDNA) 391819-92-4 391820-03-4, DNA (human clone 23759
       391820-04-5, DNA (human clone 23693 cDNA) · 391820-05-6, DNA
cDNA)
(human clone 23732 cDNA) 391820-14-7, DNA (human clone 23748 cDNA)
391821-01-5
            391821-35-5
                         391821-43-5 391821-88-8
                                                    391822-29-0
391822-53-0
             391822-85-8 391822-86-9, DNA (human clone 2.1 cDNA)
391824-41-2
           391826-32-7
                          391826-61-2, DNA (human gene MDFI cDNA)
391826-94-1 391826-95-2
                          391827-04-6, DNA (human gene Kir1.3)
391827-16-0 391827-18-2 391827-29-5, DNA (human gene TSG101 cDNA)
391828-27-6, DNA (human semaphorin E cDNA) 391828-94-7 391829-27-9,
```

```
DNA (human gene SUPT5H cDNA)
                              391830-45-8, DNA (human gene MIP-3β
        391830-79-8
                     391831-34-8, DNA (human cell line CEM cells cDNA)
             391831-69-9
                           391831-70-2, DNA (human A28-RGS14p cDNA)
391831-38-2
391831-77-9, DNA (human cell line LIM1215 cDNA)
                                                 391831-82-6
             391831-89-3, DNA (human gene HTP-1 cDNA)
                                                         391832-05-6
391831-88-2
391832-06-7, DNA (human gene VRK2 cDNA)
                                         391832-46-5, DNA (human gene
        391832-48-7
                     391832-75-0, DNA (human nucleolar protein
           391832-90-9
                          391833-04-8, DNA (human clone RES4-22B cDNA)
p40 cDNA)
391833-06-0, DNA (human clone RES4-26 cDNA)
                                              391833-38-8, DNA (human glia
                         391833-54-8, GenBank Y09561
                                                        391833-55-9
maturation factor cDNA)
             391833-85-5
                           391834-62-1
                                         391835-20-4
391833-60-6
                                                        391835-95-3, DNA
(human clone phKII-3 cDNA)
                            391835-97-5
                                          391835-98-6, GenBank X99886
                          391836-06-9, DNA (human clone HP01049 cDNA)
391836-00-3
              391836-02-5
              391836-20-7, DNA (human clone 23907 cDNA)
391836-14-9
                                                          391836-80-9, DNA
                        391836-81-0, DNA (human HS1 binding
(human gene CDS cDNA)
protein cDNA)
               391836-99-0
                            391837-13-1, DNA (human gene cul-2
                                                    391838-71-4
        391838-09-8, DNA (human clone 31293 cDNA)
391839-11-5
              391839-14-8
                            391839-27-3, DNA (human HYA22 cDNA)
391839-32-0
             391840-69-0, DNA (human gene DRADA2b cDNA)
                                                           391840-75-8
391840-93-0, DNA (human pyridoxal kinase cDNA)
                                                 391840-94-1
             391841-59-1, DNA (human clone ATCC 353794 cDNA)
391841-52-4
391841-60-4, DNA (human gene UCPH cDNA)
                                         391841-63-7
                                                        391842-02-7
                            391842-52-7
                                         391842-76-5
                                                        391843-15-5
391842-07-2
              391842-29-8
                            391844-49-8, DNA (human gene NPT4 cDNA)
391843-44-0
              391844-43-2
391844-53-4, DNA (human gene BTF2)
                                   391844-55-6, DNA (human gene BTF5
                     391845-63-9, DNA (human bikunin cDNA)
                                                              391845-65-1,
       391844-65-8
                            391845-67-3, GenBank U96115
                                                          391846-71-2
DNA (human gene OPG cDNA)
                            391847-56-6, DNA (human Hlark cDNA)
             391847-29-3
391846-81-4
391848-63-8, DNA (human clone R31396-F25451-R31076 )
                                                       391849-10-8
391849-11-9
              391850-10-5
                            391851-20-0
                                         391851-69-7
                                                        391851-70-0
                            391853-04-6
391852-01-0
                                          391853-23-9, DNA (human gene HE6
              391852-23-6
                                   391854-48-1
                                                 391854-67-4
        391853-60-4 391854-27-6
cDNA)
391854-98-1, DNA (human transmembrane protein cDNA)
391854-99-2, DNA (human protein IPL cDNA plus flanks)
              391856-28-3
                                         391857-86-6
                            391856-63-6
                                                        391982-57-3
391856-09-0
                            391984-57-9
                                          391984-90-0
                                                        391985-36-7
391983-35-0
              391984-34-2
              391985-57-2
                            391985-88-9
                                          391986-15-5
                                                        391986-21-3
391985-53-8
                            391987-27-2
                                          391987-58-9
                                                        391987-78-3
              391987-11-4
391986-25-7
                                   391989-61-0
                                                   391989-66-5
391988-89-9, DNA (human gene BCL9)
              391990-27-5 391990-29-7
                                         391990-30-0
                                                        391991-74-5
391989-94-9
              391992-17-9, DNA (human clone genomic t083 )
                                                             391995-75-8
391992-10-2
              391997-75-4
                            391998-54-2
                                         391998-85-9
                                                        391999-44-3
391997-52-7
                                          392002-24-3
                            392000-73-6
                                                        392003-69-9
              392000-55-4
391999-46-5
                                                         392004-89-6
392003-98-4, DNA (human gene hPARG cDNA)
                                           392004-66-9
              392007-47-5, DNA (human gene hCTR1 cDNA)
                                                        392009-64-2, DNA
392005-83-3
(human clone ICRFc103G087 )
                             392009-77-7, DNA (human cell line HeLa S3
                     392011-03-9, DNA (human gene OB-RGRP cDNA)
        392010-66-1
              392011-10-8, DNA (human gene selW cDNA)
392011-08-4
                                                        392012-11-2
              392012-21-4, DNA (human DEC1 cDNA)
                                                   392013-07-9
392012-20-3
              392015-53-1, GenBank AJ000099
                                              392015-75-7
392013-09-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
   (nucleotide sequence; expressed gene sets as markers for specific
   tumors)
                            392020-66-5
                                          392069-90-8, DNA (human
              392019-08-8
392017-13-9
                     392109-74-9
                                   392110-12-2, DNA (human gene
αB-crystallin cDNA)
                   392185-63-6, DNA (human glutaminyl-tRNA synthetase)
antiquitin cDNA)
392186-08-2, DNA (human serotonin receptor gene) 392192-85-7
            392193-15-6, DNA (human gene ATPL cDNA) 392193-18-9
392193-09-8
                                   392193-44-1 392193-62-3, GenBank
392193-30-5, DNA (human gene CGM7)
```

```
392193-80-5
                      392194-85-3
                                    392195-25-4
                                                  392195-88-9
392198-67-3
             392198-83-3, DNA (human clone hg00112s1 cDNA)
                                                             392198-94-6
392199-04-1
             392202-92-5
                           392204-42-1, DNA (human protein p85
       392204-45-4 392204-50-1
                                  392204-58-9
                                                392204-69-2
            392204-97-6, DNA (human clone HG1758 cDNA)
392204-88-5
                                                          392205-48-0
392207-45-3, DNA (human gene IGFBP6 cDNA)
                                           392207-71-5, DNA (human clone
hh00141s1 cDNA)
                 392208-97-8, DNA (human clone lambdaF2.6 cDNA)
392209-02-8, DNA (human gene IGFBP4 cDNA)
                                          392209-77-7, DNA (human clone
              392213-11-5
                            392213-13-7
                                         392213-15-9, DNA (human gene
HH0733 cDNA)
             392214-43-6, GenBank M31776 392214-46-9, GenBank J00212
IGF1R cDNA)
                             398095-16-4, DNA (human clone lambda hK1R
392214-97-0, GenBank M88579
       398095-28-8
                    398095-31-3, DNA (human preproinsulin gene)
398095-63-1, DNA (human \alpha-tubulin gene)
                                         398096-95-2, DNA (human
                        398109-70-1, GenBank D21241
gene ACY1 protein cDNA)
398109-87-0 398110-85-5, DNA (human gene PKD1 cDNA)
                                                       398113-74-1, DNA
                       398113-83-2, DNA (human cell line W138 cell line
(human gene FXR2 cDNA)
                                         398425-27-9, DNA (human gene
    398114-34-6, DNA (human Smad6 cDNA)
        398425-36-0
                     398425-42-8 398425-46-2, DNA (human gene NAGA
IL1R)
CDNA)
        398425-50-8, GenBank M20778 398425-55-3, DNA (human gene GRP
        398425-70-2 398425-86-0, DNA (human cell line U118-MG cDNA)
CDNA)
398426-03-4, DNA (human gene STS cDNA)
                                       398426-09-0
                                                      398426-14-7, DNA
(human gene BDH cDNA)
                      398435-07-9 398448-49-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
   (nucleotide sequence; expressed gene sets as markers for specific
   tumors)
```

- L40 ANSWER 39 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2001:912134 HCAPLUS
- DN 137:61092
- ED Entered STN: 18 Dec 2001
- TI MCF-10A-NeoST: a new cell system for studying cell-ECM and cell-cell interactions in breast cancer
- AU Zantek, Nicole Dodge; Walker-Daniels, Jennifer; Stewart, Jane; Hansen, Rhonda K.; Robinson, Daniel; Miao, Hui; Wang, Bingcheng; Kung, Hsing-Jien; Bissell, Mina J.; Kinch, Michael S.
- CS Department of Basic Medical Sciences, Purdue University, West Lafayette, IN, 47905, USA
- SO Clinical Cancer Research (2001), 7(11), 3640-3648 CODEN: CCREF4; ISSN: 1078-0432
- PB American Association for Cancer Research
- DT Journal
- LA English
- CC 14-1 (Mammalian Pathological Biochemistry)
- There is a continuing need for genetically matched cell systems to model AB cellular behaviors that are frequently observed in aggressive breast cancers. We report here the isolation and initial characterization of a spontaneously arising variant of MCF-10A cells, NeoST, which provides a new model to study cell adhesion and signal transduction in breast cancer. NeoST cells recapitulate important biol. and biochem. features of metastatic breast cancer, including anchorage-independent growth, invasiveness in three-dimensional reconstituted membranes, loss of E-cadherin expression, and increased tyrosine kinase activity. A comprehensive anal. of tyrosine kinase expression revealed overexpression or functional activation of the Axl, FAK, and EphA2 tyrosine kinases in transformed MCF-10A cells. MCF-10A and these new derivs. provide a genetically matched model to study defects in cell adhesion and signaling that are relevant to cellular behaviors that often typify aggressive breast cancer cells.

```
ST
    breast cancer disease model MCF10A NeoST; cell adhesion breast cancer
    disease model; signal transduction breast cancer disease model
TT
    Cadherins
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (E-; MCF-10A-NeoST: new cell system for studying cell-ECM and cell-cell
        interaction in breast cancer)
IT
    Adhesion, biological
    Disease models
    Extracellular matrix
    Mammary gland, neoplasm
     Signal transduction, biological
        (MCF-10A-NeoST: new cell system for studying cell-ECM and cell-cell
        interaction in breast cancer)
IT
    Growth, animal
        (anchorage-independent; MCF-10A-NeoST: new cell system for studying
        cell-ECM and cell-cell interaction in breast cancer)
IT
    Neoplasm
        (metastasis; MCF-10A-NeoST: new cell system for studying cell-ECM and
        cell-cell interaction in breast cancer)
     80449-02-1, Tyrosine kinase
IT
                                  144114-16-9, Focal
     adhesion kinase 149433-91-0, EphA2
                               153190-63-7, Axl
    receptor tyrosine kinase
    receptor tyrosine kinase
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (MCF-10A-NeoST: new cell system for studying cell-ECM and cell-cell
        interaction in breast cancer)
              THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RE
(1) Bae, S; Breast Cancer Res Treat 1993, V24, P241 MEDLINE
(2) Bartley, T; Nature (Lond) 1994, V368, P558 HCAPLUS
(3) Bellosta, P; Oncogene 1997, V15, P2387 HCAPLUS
(4) Birchmeier, W; Bioessays 1995, V17, P97 HCAPLUS
(5) Bissell, M; Am J Pathol 1999, V155, P675 MEDLINE
(6) Bissell, M; Cancer Res 1999, V59, P1757 MEDLINE
(7) Briand, P; Cancer Res 1996, V56, P2039 HCAPLUS
(8) Burchert, A; Oncogene 1998, V16, P3177 HCAPLUS
(9) Burridge, K; Annu Rev Cell Dev Biol 1996, V12, P463 HCAPLUS
(10) Burridge, K; J Cell Biol 1992, V119, P893 HCAPLUS
(11) Calderwood, D; J Biol Chem 2000, V275, P22607 HCAPLUS
(12) Cance, W; Breast Cancer Res Treat 1995, V35, P105 HCAPLUS
(13) Clark, G; Oncogene 1996, V12, P169 HCAPLUS
(14) Coppolino, M; Int J Biochem Cell Biol 2000, V32, P171 HCAPLUS
(15) Davis, S; Science (Wash DC) 1994, V266, P816 HCAPLUS
(16) Fidler, I; J Natl Cancer Inst (Bethesda) 1996, V88, P1700 MEDLINE
(17) Fridell, Y; J Biol Chem 1998, V273, P7123 HCAPLUS
(18) Frisch, S; Curr Opin Cell Biol 1997, V9, P701 HCAPLUS
(19) Garbe, J; Oncogene 1999, V18, P2169 HCAPLUS
(20) Goruppi, S; Mol Cell Biol 2001, V21, P902 HCAPLUS
(21) Graff, J; Cancer Res 1998, V58, P2063 HCAPLUS
(22) Hess, A; Cancer Res 2001, V61, P3250 HCAPLUS
(23) Hunter, T; Cell 1997, V88, P333 HCAPLUS
(24) Janssen, J; Oncogene 1991, V6, P2113 HCAPLUS
(25) Kinch, M; Biochem Soc Trans 1995, V23, P446 HCAPLUS
(26) Kinch, M; Hybridoma 1998, V17, P227 HCAPLUS
(27) Kinch, M; J Cell Biol 1995, V130, P461 HCAPLUS
(28) Kornberg, L; J Biol Chem 1992, V267, P23439 HCAPLUS
(29) Lawrence, J; World J Urol 1996, V14, P124 MEDLINE
```

(30) Lee, W; Mol Cell Biol 1999, V19, P8075 HCAPLUS

(31) Levitzki, A; Science (Wash DC) 1995, V267, P1782 HCAPLUS (32) Li, L; J Natl Cancer Inst (Bethesda) 1989, V81, P1406 MEDLINE

- haddad 10 / 823259 (33) Lin, W; Oncogene 2000, V19, P5680 HCAPLUS (34) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS (35) Ling, L; Mol Cell Biol 1995, V15, P6582 HCAPLUS (36) Lochter, A; Semin Cancer Biol 1995, V6, P165 HCAPLUS (37) Maher, P; Proc Natl Acad Sci USA 1985, V82, P6576 HCAPLUS (38) Maniotis, A; Am J Pathol 1999, V155, P739 MEDLINE (39) Miao, H; Nature Cell Biol 2000, V2(2), P62 HCAPLUS (40) Miller, F; J Natl Cancer Inst (Bethesda) 1993, V85, P1725 MEDLINE (41) O'Bryan, J; Mol Cell Biol 1991, V11, P5016 HCAPLUS (42) Parsons, J; Important Adv Oncol 1993, P3 MEDLINE (43) Parsons, J; J Cell Sci Suppl 1994, V18, P109 HCAPLUS (44) Pauley, R; Eur J Cancer Prev 1993, V3 (Suppl 2), P67 (45) Petersen, O; Proc Natl Acad Sci USA 1992, V89, P9064 MEDLINE (46) Price, J; Breast Cancer Res Treat 1996, V39, P93 MEDLINE (47) Ruoslahti, E; Adv Cancer Res 1999, V76, P1 HCAPLUS (48) Ruoslahti, E; Princess Takamatsu Symp 1994, V24, P99 MEDLINE (49) Schaller, M; Proc Natl Acad Sci USA 1992, V89, P5192 HCAPLUS (50) Schlaepfer, D; Trends Cell Biol 1998, V8, P151 HCAPLUS (51) Schmeichel, K; J Mammary Gland Biol & Neoplasia 1998, V3, P201 MEDLINE (52) Schoenwaelder, S; Curr Opin Cell Biol 1999, V11, P274 HCAPLUS (53) Stampfer, M; Mol Biol Cell 1997, V8, P2391 HCAPLUS (54) Steeg, P; Am J Pathol 1996, V149, P733 HCAPLUS (55) Sternlicht, M; Cell 1999, V98, P137 HCAPLUS (56) Sternlicht, M; Oncogene 2000, V19, P1102 HCAPLUS (57) Sun, X; Cell Growth Differ 1999, V10, P343 HCAPLUS (58) Vleminckx, K; Bioessays 1999, V21, P211 MEDLINE (59) Weaver, V; Semin Cancer Biol 1995, V6, P175 HCAPLUS (60) Woodhouse, E; Cancer (Phila) 1997, V80, P1529 MEDLINE (61) Zand, M; Cell Motil Cytoskeleton 1989, V13, P94 MEDLINE (62) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS (63) Zelinski, D; Cancer Res 2001, V61, P2301 HCAPLUS (64) Zhong, C; Mol Biol Cell 1997, V8, P2329 HCAPLUS L40 ANSWER 40 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN AΝ 2001:899097 HCAPLUS DN 136:260866 Entered STN: 13 Dec 2001 ED Reduced expression of Ephrin A1 (EFNA1) inhibits TΙ three-dimensional growth of HT29 colon carcinoma cells ΑIJ Potla, Lyka; Boghaert, Erwin R.; Armellino, Douglas; Frost, Philip; Damle, Nitin K. CS Oncology/Immunology Division, Wyeth-Ayerst Research, Pearl River, NY, 10965-1299, USA SO Cancer Letters (Shannon, Ireland) (2002), 175(2), 187-195 CODEN: CALEDQ; ISSN: 0304-3835 PB Elsevier Science Ireland Ltd. DT Journal LA English CC 14-1 (Mammalian Pathological Biochemistry)
- Bphrin A1 (EFNA1) is a GPI-anchored ligand that preferentially binds to the receptor tyrosine kinase,
 EphA2. EphA2 is over-expressed in malignant melanocytes and in prostate carcinoma cells. Whether activation of Eph-A2 by EFN-A1 is involved in aberrant growth or differentiation of cancer cells is currently not known. We studied the effect of reducing EFNA1 on the growth of a colon carcinoma cell line (HT29). HT29 cells were transfected with EFNA1 antisense yielding clones that expressed less than 25% of EFNA1 found in vector controls. EFNA1-antisense transfectants grew slower than controls when cultured as three-dimensional spheroids. When grown as monolayers, the transfectants had a similar doubling time of

haddad - 10 / 823259 the vector controls. These results indicated that autocrine stimulation of EphA2 by EFNA1 could trigger an indirect growth signal by overcoming 'contact inhibition'. Following addition of EFNA1-Fc to HT29 cells, tyrosine hyperphosphorylation of EphA2, E-cadherin, and β-catenin were observed Because the function of E-cadherin is associated with contact inhibition of HT29 cells, phosphorylation of E-cadherin and β -catenin by activation of EphA1 is one possible mechanism by which HT29 cells alleviate contact inhibition. ephrinAl EFNAl colon carcinoma; cadherin catenin phosphorylation cell proliferation Cadherins RL: BSU (Biological study, unclassified); BIOL (Biological study) (E-; ephrinAl-induced phosphorylation of cadherin-E, β-catenin, and EphA2 in association with cell proliferation of human colon carcinoma) Intestine, neoplasm (colon, carcinoma; ephrinAl-induced phosphorylation of cadherin-E, β-catenin, and EphA2 in association with cell proliferation of human colon carcinoma) Carcinoma (colon; ephrinA1-induced phosphorylation of cadherin-E, β-catenin, and EphA2 in association with cell proliferation

ST

IT

IT

IT

of human colon carcinoma)

IT Proteins

> RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study) (ephrin-A1; ephrinA1-induced phosphorylation of

cadherin-E, β-catenin, and EphA2 in association with cell proliferation of human colon carcinoma)

IT Cell proliferation Human

> (ephrinA1-induced phosphorylation of cadherin-E, β-catenin, and EphA2 in association with cell proliferation of human colon carcinoma)

IT Phosphorylation, biological

> (protein; ephrinAl-induced phosphorylation of cadherin-E, β-catenin, and EphA2 in association with cell proliferation of human colon carcinoma)

TТ Catenins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (β-; ephrinA1-induced phosphorylation of cadherin-E, β-catenin, and EphA2 in association with cell proliferation of human colon carcinoma)

IT 149433-91-0, EphA2 receptor tyrosine kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (ephrinAl-induced phosphorylation of cadherin-E, β-catenin, and EphA2 in association with cell proliferation of human colon carcinoma)

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Aoki, J; J Cell Biol 1991, V115, P1751 HCAPLUS
- (2) Attia, M; Cancer Res 1966, V26, P1787 MEDLINE
- (3) Brady-Kalnay, S; Int J Cancer 1992, V49, P239
- (4) DeMichelli, R; Cancer Res 1989, V49, P6543
- (5) Dorudi, S; Am J Pathol 1993, V142, P981 MEDLINE
- (6) Easty, D; Cancer Res 1995, V55, P2528 HCAPLUS
- (7) Kandikonda, S; Cell Adhes Commun 1996, V4, P13 HCAPLUS
- (8) Mucller-Klieser, W; J Cell Biol 1997, V273, P1109

```
(9) Ogawa, K; Oncogene 2000, V19, P6043 HCAPLUS
(10) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
(11) Shibamoto, S; Cell Adhes Commun 1994, V1, P295 HCAPLUS
(12) Shiozaki, H; Br J Cancer 1995, V71, P250 HCAPLUS
(13) St Croix, B; J Cell Biol 1998, V142, P557 HCAPLUS
(14) Stein, E; Genes Dev 1998, V12, P667 HCAPLUS
(15) Takeda, H; J Cell Biol 1995, V131, P1839 HCAPLUS
(16) Vleminckx, K; BioEssays 1999, V21, P211 MEDLINE
(17) Walker Daniels, W; Prostate 1999, V41, P275
(18) Watabe, M; J Cell Biol 1994, V127, P247 HCAPLUS
(19) Westermark, B; Int J Cancer 1974, V12, P438
(20) Yap, A; Annu Rev Cell Dev Biol 1997, V13, P119 HCAPLUS
(21) Yuhas, J; Cancer Res 1977, V37, P3639 MEDLINE
(22) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
T.40
     ANSWER 41 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
     2001:779727 HCAPLUS
AN
DN
     136:52021
     Entered STN: 26 Oct 2001
ED
TI
     Receptor tyrosine kinase EphA2 is
     regulated by p53-family proteins and induces apoptosis
AU
     Dohn, Michael; Jiang, Jieyuan; Chen, Xinbin
CS
     Institute of Molecular Medicine and Genetics, Medical College of Georgia,
     Augusta, GA, 30912, USA
SO
     Oncogene (2001), 20(45), 6503-6515
     CODEN: ONCNES; ISSN: 0950-9232
PB
     Nature Publishing Group
DT
     Journal
LA
     English
CC
     14-1 (Mammalian Pathological Biochemistry)
     Section cross-reference(s): 2, 3
AB
     The p53 tumor suppressor protein is mutated in more than 50% of
     all human cancers, which makes the study of its functions and activities
     critical for the understanding and management of cancer. In response to
     cellular stresses, p53 is activated and can mediate cell cycle arrest
     and/or apoptosis via the upregulation of numerous target genes. Here, the
     authors have identified EphA2 as a target gene of the p53
     family, i.e., p53, p73, and p63. The authors also found that an increase
     of EphA2 transcript levels correlated with an increase of
     EphA2 protein expression, and induction of EphA2
     in response to DNA damage corresponded with p53 activation. Furthermore,
     the authors identified a p53 response element located within the
     EphA2 promoter that is responsive to wild-type p53, p73, and p63,
     but not mutant p53. Interestingly, the ligand for EphA2,
     ephrin-A1, is also regulated by p53. EphA2 and
     ephrin-Al are members of the Eph family of
     receptor tyrosine kinases and ligands, which
     are implicated in a number of developmental processes. To analyze the role
     of EphA2 in p53-mediated tumor suppression, the authors
     generated stable cell lines capable of expressing exogenous EphA2
     in a tetracycline-repressible system. The authors found that
     EphA2 expression resulted in an increase in apoptosis. Thus, the
     authors hypothesize that the activated EphA2 may serve to impair
     anti-apoptotic signaling, perhaps by disrupting focal adhesions and
     thereby sensitize cells to pro-apoptotic stimuli.
ST
     receptor tyrosine kinase EphA2 p53
     family apoptosis tumor suppression
IT
     Tyrosine kinase receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
```

(EphA2; receptor tyrosine kinase

```
EphA2 is regulated by p53-family proteins and induces
        apoptosis in relation to tumor suppression)
TΤ
     Gene, animal
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (EphA2; receptor tyrosine kinase
        EphA2 is regulated by p53-family proteins and induces
        apoptosis in relation to tumor suppression)
IT
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); BIOL (Biological study)
        (damage; receptor tyrosine kinase
        EphA2 is regulated by p53-family proteins and induces
        apoptosis in relation to tumor suppression and DNA damage-induced
        EphA2 phosphorylation)
     Growth factors, animal
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ephrin-A1; receptor tyrosine
        kinase EphA2 is regulated by p53-family
        proteins and induces apoptosis in relation to tumor suppression
        and)
     Transcription factors
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (p63; receptor tyrosine kinase
        EphA2 is regulated by p53-family proteins and induces
        apoptosis in relation to tumor suppression)
     Transcription factors
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (p73; receptor tyrosine kinase
        EphA2 is regulated by p53-family proteins and induces
        apoptosis in relation to tumor suppression)
IT
     Animal cell line
     Apoptosis
     Human
     Neoplasm
     Transcription, genetic
        (receptor tyrosine kinase EphA2
        is regulated by p53-family proteins and induces apoptosis in
        relation to tumor suppression)
IT
     mRNA
     p53 (protein)
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
         (receptor tyrosine kinase EphA2
        is regulated by p53-family proteins and induces apoptosis in
        relation to tumor suppression)
     Phosphorylation, biological
TT
         (receptor tyrosine kinase EphA2
        is regulated by p53-family proteins and induces apoptosis in
        relation to tumor suppression and DNA damage-induced EphA2
        phosphorylation)
     Promoter (genetic element)
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
      (Biological study)
         (receptor tyrosine kinase EphA2
         is regulated by p53-family proteins and induces apoptosis in
        relation to tumor suppression and p53-responsive element in
        EphA2 promoter)
IT
     Genetic element
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
      (Biological study)
```

(tumor antigen p53-responsive element; receptor tyrosine kinase EphA2 is regulated by p53-family proteins and induces apoptosis in relation to tumor suppression and p53-responsive element in EphA2 promoter)

IT 149433-91-0, EphA2 receptor tyrosine

RL: BSU (Biological study, unclassified); BIOL (Biological study) (receptor tyrosine kinase EphA2 is regulated by p53-family proteins and induces apoptosis in relation to tumor suppression)

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Agarwal, M; J Biol Chem 1998, V273, P1 HCAPLUS
- (2) Bartley, T; Nature 1994, V368, P558 HCAPLUS
- (3) Candau, R; Oncogene 1997, V15, P807 HCAPLUS
- (4) Chen, C; Mol Cell Biol 1987, V7, P2745 HCAPLUS
- (5) Chen, X; Genes Dev 1996, V10, P2438 HCAPLUS
- (6) Chen, X; Mol Med Today 1999, V5, P387 HCAPLUS
- (7) Cheng, H; Cell 1995, V82, P371 HCAPLUS
- (8) Committee, E; Cell 1997, V90, P403
- (9) de Laurenzi, V; Cell Death Differ 1999, V6, P389 HCAPLUS
- (10) de Laurenzi, V; J Exp Med 1998, V188, P1763 HCAPLUS
- (11) Dohn, M; Oncogene 2001, V20, P3193 HCAPLUS
- (12) El-Deiry, W; Cell 1993, V75, P817 HCAPLUS
- (13) El-Deiry, W; Nat Genet 1992, V1, P45 HCAPLUS
- (14) Flanagan, J; Annu Rev Neurosci 1998, V21, P309 HCAPLUS
- (15) Frisch, S; J Cell Biol 1996, V134, P793 HCAPLUS
- (16) Frisen, J; EMBO J 1999, V18, P5159 HCAPLUS
- (17) Frisen, J; Neuron 1998, V20, P235 HCAPLUS
- (18) Gale, N; Neuron 1996, V17, P9 HCAPLUS
- (19) Guilford, P; Mol Med Today 1999, V5, P172 HCAPLUS
- (20) Gumbiner, B; Cell 1996, V84, P345 HCAPLUS
- (21) Harper, J; Cell 1993, V75, P805 HCAPLUS
- (22) Henkemeyer, M; Cell 1996, V86, P35 HCAPLUS
- (23) Holder, N; Development 1999, V126, P2033 HCAPLUS
- (24) Hollstein, M; Nucleic Acids Res 1994, V22, P3551 HCAPLUS
- (25) Hollstein, M; Science 1991, V253, P49 HCAPLUS
- (26) Hungerford, J; J Cell Biol 1996, V135, P1383 HCAPLUS
- (27) Ilic, D; J Cell Biol 1998, V143, P547 HCAPLUS
- (28) Johansen, F; Mol Cell Biol 1994, V14, P5920 HCAPLUS
- (29) Jost, C; Nature 1997, V389, P191 HCAPLUS
- (30) Kaelin, W; Oncogene 1999, V18, P7701 HCAPLUS
- (31) Kaghad, M; Cell 1997, V90, P809 HCAPLUS
- (32) Levine, A; Cell 1997, V88, P323 HCAPLUS
- (33) Levrero, M; J Cell Sci 2000, V113, P1661 HCAPLUS
- (34) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
- (35) Mellitzer, G; Nature 1999, V400, P77 HCAPLUS
- (36) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
- (37) Miao, H; Nat Cell Biol 2001, V3, P527 HCAPLUS
- (38) Miyashita, T; Cell 1995, V80, P293 HCAPLUS
- (39) Osada, M; Nat Med 1998, V4, P839 HCAPLUS
- (40) Ozaki, T; Cancer Res 1999, V59, P5902 HCAPLUS
- (41) O'Leary, D; Curr Opin Neurobiol 1999, V9, P65 HCAPLUS
- (42) Prives, C; J Pathol 1999, V187, P112 HCAPLUS
- (43) Rodriguez-Fernandez, J; Bioessays 1999, V21, P1069 MEDLINE
- (44) Scheffner, M; Cell 1993, V75, P495 HCAPLUS
- (45) Schmale, H; Oncogene 1997, V15, P1363 HCAPLUS
- (46) Senoo, M; Biochem Biophys Res Commun 1998, V248, P603 HCAPLUS
- (47) Shimada, A; Cancer Res 1999, V59, P2781 HCAPLUS

```
(48) Smith, C; J Biol Chem 1997, V272, P27493 HCAPLUS
(49) Sonoda, Y; J Biol Chem 2000, V275, P16309 HCAPLUS
(50) Trink, B; Nat Med 1998, V4, P747
(51) Ueda, Y; Oncogene 1999, V18, P4993 HCAPLUS
(52) van der Geer, P; Annu Rev Cell Biol 1994, V10, P251 HCAPLUS
(53) Xu, Q; Nature 1999, V399, P267 HCAPLUS
(54) Yang, A; Mol Cell 1998, V2, P305 HCAPLUS
(55) Yang, A; Nat Rev Mol Cell Biol 2000, V1, P199 HCAPLUS
(56) Yang, A; Nature 2000, V404, P99 HCAPLUS
(57) Yu, J; Proc Natl Acad Sci USA 1999, V96, P14517 HCAPLUS
(58) Zaika, A; Cancer Res 1999, V59, P3257 HCAPLUS
(59) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
(60) Zhao, R; Genes Dev 2000, V14, P981 HCAPLUS
(61) Zhu, J; Cancer Res 1998, V58, P5061 HCAPLUS
(62) Zhu, J; J Biol Chem 1998, V273, P13030 HCAPLUS
(63) Zhu, J; Mol Cell Biol 2000, V20, P5602 HCAPLUS
(64) Zhu, K; Oncogene 1999, V18, P7740 HCAPLUS
L40
    ANSWER 42 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
    2001:721437 HCAPLUS
AN
DN
    135:272896
    Entered STN: 03 Oct 2001
ED
    Preparation of substituted 3-cyanoquinolines as protein
TТ
    tyrosine kinases inhibitors
    Wissner, Allan; Tsou, Hwei-ru; Berger, Dan M.; Floyd, Middleton B., Jr.;
IN
    Hamann, Philip R.; Zhang, Nan; Frost, Philip
    American Cyanamid Company, USA
PA
    U.S., 57 pp., Cont. of U.S. Ser. No. 405,868, abandoned.
SO
    CODEN: USXXAM
DT
    Patent
LΑ
    English
    ICM A61K031-47
IC
    ICS C07D215-44
INCL 514313000
    27-17 (Heterocyclic Compounds (One Hetero Atom))
    Section cross-reference(s): 1, 63
FAN.CNT 1
    PATENT NO.
                       KIND
                             DATE
                                         APPLICATION NO.
                                                               DATE
                                          -----
     -----
                       ----
                               -----
                                        US 2000-630270
                                                                20000801 <--
    US 6297258
                        В1
                               20011002
PRAI US 1998-150699P
                        Р
                               19980929 <--
    US 1999-405868
                        B1
                              19990924 <--
CLASS
               CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
 -----
                       ______
 US 6297258
                IÇM
                       A61K031-47
                ICS
                       C07D215-44
                INCL
                       514313000
                       514/313.000; 514/151.000; 514/228.200; 514/235.200;
 US 6297258
                NCL
                       514/252.180; 514/253.060; 514/253.070; 514/278.000;
                       514/312.000; 544/058.600; 544/128.000; 544/328.000;
                       544/331.000; 544/363.000; 546/019.000; 546/153.000;
                       546/159.000; 546/160.000; 546/171.000
                       C07D215/44
                ECLA
    MARPAT 135:272896
OS
GT
```

$$G^1$$
 G^2
 R^1
 Z
 CN
 CN
 R^2
 R^4
 R^4

MeO
$$C \equiv C$$
 M M CN M

AB Title compds. I [X = cycloalkyl, pyridinyl, pyrimidinyl, etc.; Z = NH, O, . S, NR; R = alkyl; G1, G2, R1, R4 = H, halo, alkyl, alkynyl, etc.; n = 0, 1], protein tyrosine kinase inhibitors, were prepared Examples included 189 compds. and 6 bioassays. E.g., II was prepared by coupling the 4-(2-methoxyethoxy)but-2-ynoic acid with 6-amino-3-cyano-4-[(3-bromophenyl)amino]quinoline

II

(i-BuOCOCl, N-methylmorpholine, THF, 0°C, 3 h) in 32% yield after purification II had IC50 = 0.006 μ M for EGFR kinase. I are useful as antineoplastic agents.

ST cyanoquinoline prepn protein tyrosine kinase inhibitor; quinoline cyano prepn protein tyrosine kinase inhibitor; antineoplastic

agent cyanoquinoline prepn

IT Antitumor agents

(preparation of cyanoquinolines as antineoplastic agents)

IT 79079-06-4, Epidermal growth factor receptor kinase

137632-08-7, ERK 2 kinase 142805-58-1, MAPKK

149433-91-0, **Eck kinase** 150977-45-0, KDR

receptor tyrosine kinase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(preparation of cyanoquinolines as antineoplastic agents)

IT 198149-15-4P 263148-94-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of cyanoquinolines as protein tyrosine kinase inhibitors)

```
IT
     2103-50-6P
                  214476-89-8P
                                  214476-99-0P
                                                 263148-87-4P
                                                                 263148-88-5P
     263148-89-6P
                    263148-90-9P
                                    263148-91-0P
                                                   263148-92-1P
                                                                   263148-93-2P
     263148-95-4P
                    263148-98-7P
                                    263149-00-4P
                                                   263149-01-5P
                                                                   263149-02-6P
     263149-03-7P
                                                   263149-07-1P
                    263149-04-8P
                                    263149-06-0P
                                                                   263149-08-2P
     263149-09-3P
                    263149-10-6P
                                    263149-11-7P
                                                   263149-12-8P
                                                                   263149-13-9P
     263149-14-0P
                    263149-16-2P
                                    263149-17-3P
                                                   263149-18-4P
                                                                   263149-19-5P
     263149-20-8P
                    263149-26-4P
                                    263149-30-0P
                                                   263149-31-1P
                                                                   263149-32-2P
     263149-33-3P
                    263149-34-4P
                                    263149-35-5P
                                                   263149-36-6P
                                                                   263149-37-7P
```

```
263149-38-8P
              263149-39-9P
                             263149-40-2P
                                            263149-41-3P
                                                           263149-42-4P
263149-43-5P
              263149-44-6P
                             263149-45-7P
                                            263149-46-8P
                                                           263149-47-9P
263149-48-0P
              263149-49-1P
                             263149-50-4P
                                            263149-51-5P
                                                           263149-52-6P
263149-54-8P
              263149-57-1P
                             263149-60-6P
                                            263149-63-9P
                                                           263149-66-2P
263149-68-4P
              263149-69-5P
                             263149-70-8P
                                            263149-72-0P
                                                           263149-74-2P
263149-75-3P
              263149-77-5P
                             263149-79-7P
                                            263149-81-1P
                                                           263149-83-3P
263149-85-5P
              263149-87-7P
                             263149-90-2P
                                            263149-92-4P
                                                           263149-95-7P
263149-98-0P
              263150-01-2P
                             263150-03-4P
                                            263150-04-5P
                                                           263150-05-6P
263150-06-7P
              263150-07-8P
                             263150-08-9P
                                            263150-09-0P
                                                           263150-10-3P
263150-11-4P
              263150-12-5P
                             263150-13-6P
                                            263150-14-7P
                                                           263150-15-8P
                             263150-18-1P
263150-16-9P
              263150-17-0P
                                            263150-20-5P
                                                           263150-22-7P
263150-24-9P
              263150-26-1P
                             263150-28-3P
                                            263150-30-7P
                                                           263150-31-8P
263150-32-9P
              263150-34-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
   (preparation of cyanoquinolines as protein tyrosine
  kinase inhibitors)
94-05-3
        97-52-9, 2-Methoxy-4-nitroaniline 98-16-8,
3-Trifluoromethylaniline 99-52-5 100-01-6, 4-Nitroaniline, reactions
103-76-4, 4-(2-Hydroxyethyl)piperazine 106-40-1, 4-Bromoaniline
106-96-7, Propargyl bromide 107-19-7, Propargyl alcohol 107-30-2,
Chloromethyl methyl ether 107-94-8, 3-Chloropropionic acid
                                                              108-42-9,
                108-44-1, 3-Toluidine, reactions 109-01-3,
3-Chloroaniline
1-Methylpiperazine 109-83-1, 2-(Methylamino)ethanol
                                                       109-86-4,
                110-97-4, 1,1'-Iminodi-2-propanol
2-Methoxyethanol
                                                      111-42-2,
Bis(2-hydroxyethyl)amine, reactions 111-95-5 123-90-0, Thiomorpholine
124-02-7, Diallylamine 177-11-7, 1,4-Dioxa-8-azaspiro[4.5]decane
367-21-5, 3-Chloro-4-fluoroaniline 504-78-9, Thiazolidine 536-90-3,
3-Methoxyaniline 590-93-2, 2-Butynoic acid 591-19-5, 3-Bromoaniline
615-55-4, 3,4-Dibromoaniline 621-33-0, 3-Ethoxyaniline
                                                          624-65-7.
                   626-01-7, 3-Iodoaniline 656-64-4,
Propargyl chloride
3-Bromo-4-fluoroaniline
                         693-95-8, 4-Methylthiazole
                                                     766-17-6,
                           1117-71-1, Methyl 4-bromocrotonate
cis-2,6-Dimethylpiperidine
2237-30-1, 3-Aminobenzonitrile 2629-72-3, 3-(4-Pyridyl)-1-propanol
2799-21-5, (R)-3-Pyrrolidinol
                               2835-95-2, 3-Hydroxy-4-methylaniline
3378-71-0, 2,5-Dimethylpyrrolidine
                                    3433-37-2, 2-Hydroxymethylpiperidine
3581-89-3, 5-Methylthiazole 3863-11-4, 3,4-Difluoroaniline
                                                             4606-65-9,
                          4747-21-1, Isopropylmethylamine
3-Hydroxymethylpiperidine
                                                             5231-87-8
5344-27-4, 2-(4-Pyridyl)ethanol 5382-16-1, 4-Hydroxypiperidine
6139-84-0, 4-Chlorobutanal
                           7223-38-3, 1-Dimethylamino-2-propyne
32631-26-8
           38256-93-8
                        41775-76-2, 1,4,7-Trioxa-10-azacyclododecane
41979-39-9, 4-Piperidone hydrochloride 51544-74-2, 4-Bromocrotonyl
chloride 54060-30-9, 3-Ethynylaniline 57366-77-5 57946-56-2,
4-Chloro-2-fluoroaniline 61032-42-6
                                                  74024-49-0
                                      63126-47-6
214470-55-0
RL: RCT (Reactant); RACT (Reactant or reagent)
   (preparation of cyanoquinolines as protein tyrosine
  kinase inhibitors)
           13280-03-0P
                          20629-35-0P 27333-44-4P
2458-24-4P
                                                      45813-02-3P
             118764-05-9P
                            214470-27-6P
71083-64-2P
                                           214470-33-4P
                                                          214470-35-6P
214470-37-8P
              214471-15-5P
                             214471-46-2P
                                            214476-07-0P
                                                           214476-08-1P
              214476-14-9P
                             214476-23-0P
214476-09-2P
                                            214484-01-2P
                                                           214484-03-4P
214484-09-0P
              214484-11-4P
                             214484-17-0P
                                            214484-18-1P
                                                           214484-20-5P
214484-21-6P
              214484-70-5P
                             214484-74-9P
                                            214484-75-0P
                                                           214484-76-1P
214484-77-2P
              214484-78-3P
                             214484-90-9P
                                            214484-91-0P
                                                           214484-93-2P
214484-94-3P
              214484-96-5P
                             214484-97-6P
                                            214485-01-5P
                                                           214485-08-2P
214485-09-3P
              214485-11-7P
                             214485-12-8P
                                            214485-14-0P
                                                           214485-15-1P
214485-17-3P
                                            214485-22-0P
              214485-18-4P
                             214485-21-9P
                                                           214485-26-4P
214485-27-5P
              214485-52-6P
                             214485-53-7P
                                            214485-59-3P
                                                           214485-60-6P
```

ΙT

IT

```
214485-64-0P
                    214485-65-1P
                                   214485-68-4P
                                                   214485-69-5P
                                                                  214485-74-2P
     214485-75-3P
                    214487-27-1P
                                   214489-60-8P
                                                   220699-97-8P
                                                                  220699-98-9P
     220699-99-0P
                    220700-00-5P
                                   220700-02-7P
                                                   220700-03-8P
                                                                  220700-04-9P
     220700-05-0P
                    263149-21-9P
                                   263149-22-0P
                                                   263149-23-1P
                                                                  263149-24-2P
     263149-25-3P
                    263149-27-5P
                                   263149-28-6P
                                                   263149-29-7P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of cyanoquinolines as protein tyrosine
        kinase inhibitors)
IT
     214485-81-1P
                    214487-06-6P
                                   263148-96-5P
                                                   263148-97-6P
                                                                  263148-99-8P
     263150-36-3P
                    263150-38-5P
                                   263150-40-9P
                                                   263150-42-1P
                                                                  263150-44-3P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of cyanoquinolines as protein tyrosine
        kinase inhibitors)
RE.CNT
              THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
       36
RE
(1) Anon; EP 0520722 1992 HCAPLUS
(2) Anon; EP 0566226 1993 HCAPLUS
(3) Anon; EP 0602851 1994 HCAPLUS
(4) Anon; EP 0635498 1995 HCAPLUS
(5) Anon; EP 0635507 1995 HCAPLUS
(6) Anon; WO 9515758 1995 HCAPLUS
(7) Anon; WO 9519774 1995 HCAPLUS
(8) Anon; WO 9519970 1995 HCAPLUS
(9) Anon; WO 9521613 1995 HCAPLUS
(10) Anon; WO 9523141 1995 HCAPLUS
(11) Anon; WO 9524190 1995 HCAPLUS
(12) Anon; WO 9609294 1996 HCAPLUS
(13) Anon; WO 9633977 1996 HCAPLUS
(14) Anon; WO 9633978 1996 HCAPLUS
(15) Anon; WO 9633979 1996 HCAPLUS
(16) Anon; WO 9633980 1996 HCAPLUS
(17) Anon; WO 9633981 1996 HCAPLUS
(18) Anon; WO 9802434 1998 HCAPLUS
(19) Anon; WO 9802438 1998 HCAPLUS
(20) Anon; WO 9813350 1998 HCAPLUS
(21) Anon; WO 9843960 1998 HCAPLUS
(22) Bridges, A; J Med Chem 1996, V39, P267 HCAPLUS
(23) Chang, C; J Nat Prod 1992, V55, P1529 HCAPLUS
(24) Dolle, R; J Med Chem 1994, V372, P2627
(25) Du, J; Am J Physiol 1995, V269(2 Pt 1), P487
(26) Fry, D; Science 1994, V265, P1093 HCAPLUS
(27) Gattone, V; Developmental Biology 1995, V169(2), P504 HCAPLUS
(28) Gazit, A; J Med Chem 1996, V35(11), P2170
(29) Ife, R; J Med Chem 1992, V35(18), P3413 HCAPLUS
(30) Maguire, M; J Med Chem 1994, V37, P2129 HCAPLUS
(31) Nauta, J; Pediatric Research 1995, V37(6), P755 HCAPLUS
(32) Rewcastle, A; J Med Chem 1996, V39, P267
(33) Spada; US 5480883 1996 HCAPLUS
(34) Traxler; US 5686457 1997 HCAPLUS
(35) Wilson, P; Eur J Cell Biol 1993, V61(1), P131 HCAPLUS
(36) Wissner; US 6002008 1999 HCAPLUS
     ANSWER 43 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
L40
AN
     2001:672213 HCAPLUS
DN
     135:226901
ED
     Entered STN: 13 Sep 2001
TΤ
     Preparation of 3-cyanoquinolines as protein tyrosine
     kinase inhibitors
IN
     Wissner, Allan; Tsou, Hwei-ru; Berger, Dan M.; Floyd, Middleton B., Jr.;
```

```
Hamann, Philip R.; Zhang, Nan; Salvati, Mark E.; Frost, Philip
     American Cyanamid Company, USA
PΑ
SO
     U.S., 68 pp.
     CODEN: USXXAM
DT
     Patent
LA
     English
IC
     ICM A61K031-47
     ICS C07D213-68; C07D213-74
INCL 514313000
     27-17 (Heterocyclic Compounds (One Hetero Atom))
     Section cross-reference(s): 1
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                           APPLICATION NO.
                                                                  DATE
     ------
                         - - - -
                                            -----
                                -----
ΡI
    US 6288082
                         B1
                                20010911
                                           US 1999-406573
                                                                   19990924 <--
                                         <--
PRAI US 1998-150693P
                         Р
                                19980929
CLASS
 PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
 ______
                 ____
                        ------
US 6288082
                ICM
                        A61K031-47
                ICS
                        C07D213-68; C07D213-74
                INCL
                        514313000
US 6288082
                NCL
                        514/313.000; 514/234.800; 514/235.200; 514/252.180;
                        514/253.060; 514/253.070; 514/300.000; 514/312.000;
                        540/506.000; 544/112.000; 544/128.000; 544/237.000;
                        544/300.000; 544/316.000; 544/350.000; 544/354.000;
                        544/356.000; 544/363.000; 546/019.000; 546/090.000;
                        546/122.000; 546/143.000; 546/153.000; 546/159.000;
                        546/160.000; 546/162.000
                ECLA
                        C07D215/48; C07D401/12+215+209C; C07D401/12+215+211;
                        C07D401/12+233+215; C07D401/12+231+215;
                        C07D401/12+235C+215; C07D417/12+277B+215
                                                                            <--
os
    MARPAT 135:226901
GI
```

$$G^1$$
 G^2
 R^1
 C^{1}
 C^{1}
 C^{1}
 C^{2}
 C^{2}
 C^{2}
 C^{2}
 C^{2}
 C^{2}
 C^{2}
 C^{2}

ST

II

The title compds. [I; X = (un) substituted bicyclic aryl or bicyclic heteroaryl ring system of 8-12 atoms where the bicyclic heteroaryl ring contains 1-4 heteroatoms selected from N, O and S; Z = (un) substituted NH, O, S; G1, G2, R1, R4 = H, halo, alkyl, etc.; n = 0-1], useful as antineoplastic agents and in the treatment of polycystic kidney disease, were prepared Thus, Me 2-amino-4,5-diethoxybenzoate was N-condensed with HCNMe2/POCl3 and the product cyclocondensed with MeCN to give, after POCl3 treatment, 4-chloro-6,7-diethoxyquinoline-3-carbonitrile which was aminated by 6-aminoindoline to give title compd II. Data for biol. activity (inhibition of EGFR kinase, KDR, Eck, Mek-Erk) of I were given.

cyanoquinoline prepn protein tyrosine kinase

Ι

```
inhibitor antitumor; polycystic kidney disease cyanoquinoline
    prepn; mitogen activated protein kinase ERK
     inhibitor cyanoquinoline prepn; EGFR kinase
     inhibitor cyanoquinoline prepn; KDR protein
     kinase inhibitor cyanoquinoline prepn; epithelial cell
     kinase eck inhibitor cyanoquinoline prepn
IT
     Kidney, disease
        (polycystic, treatment of polycystic kidney disease; preparation of
        3-cyanoquinolines as protein tyrosine
        kinase inhibitors)
IT
    Antitumor agents
        (preparation of 3-cyanoquinolines as protein tyrosine
        kinase inhibitors)
IT
     288-32-4, Imidazole, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (Growth factor receptors preparation of 3-cyanoquinolines as
        protein tyrosine kinase inhibitors
IT
     79079-06-4, EGFR kinase
     RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL
     (Biological study)
        (mediated disorders; treatment; preparation of 3-cyanoquinolines as
        protein tyrosine kinase inhibitors
TΤ
     137632-08-7
     RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL
     (Biological study)
        (mitogen-activated protein kinase (Mek-Erk); preparation
        of 3-cyanoquinolines as protein tyrosine
        kinase inhibitors)
                                   263169-83-1P
                                                                  263169-85-3P
                    263169-82-0P
                                                   263169-84-2P
IT
     263169-81-9P
                    263169-89-7P
                                                                  263169-94-4P
     263169-87-5P
                                   263169-91-1P
                                                   263169-93-3P
     263169-95-5P
                                   263169-97-7P
                                                   263169-98-8P
                    263169-96-6P
                                                                  263169-99-9P
                                                   263170-09-8P
     263170-02-1P
                    263170-05-4P
                                   263170-08-7P
                                                                  263170-10-1P
                                   263170-13-4P
                                                   263170-14-5P
                                                                  263170-15-6P
     263170-11-2P
                    263170-12-3P
     263170-16-7P
                    263170-17-8P
                                   263170-18-9P
                                                   263170-19-0P
                                                                  263170-20-3P
                                   263170-23-6P
                                                   263170-24-7P
                                                                  263170-25-8P
     263170-21-4P
                    263170-22-5P
                                                   263170-29-2P
     263170-26-9P
                    263170-27-0P
                                   263170-28-1P
                                                                  263170-30-5P
                    263170-32-7P
                                   263170-33-8P
                                                   263170-34-9P
                                                                  263170-35-0P
     263170-31-6P
     263170-36-1P
                    263170-37-2P
                                   263170-38-3P
                                                   263170-39-4P
                                                                  263170-40-7P
     263170-41-8P
                    263170-42-9P
                                   263170-43-0P
                                                   263170-44-1P
                                                                  263170-45-2P
     263170-46-3P
                    263170-47-4P
                                   263170-48-5P
                                                   263170-49-6P
                                                                  263170-50-9P
                                                   263170-54-3P
     263170-51-0P
                    263170-52-1P
                                   263170-53-2P
                                                                  263170-55-4P
     263170-56-5P
                    263170-57-6P
                                   263170-58-7P
                                                   263170-59-8P
                                                                  263170-60-1P
     263170-61-2P
                    263170-62-3P
                                   263170-63-4P
                                                   263170-64-5P
                                                                  263170-65-6P
     263170-66-7P
                    263170-67-8P
                                   263170-68-9P
                                                   263170-69-0P
                                                                  263170-70-3P
                                                   263170-74-7P
                                                                  263170-75-8P
     263170-71-4P
                    263170-72-5P
                                   263170-73-6P
     263170-76-9P
                    263170-77-0P
                                   263170-78-1P
                                                   263170-79-2P
                                                                  263170-80-5P
                                   263170-83-8P
     263170-81-6P
                    263170-82-7P
                                                   263170-84-9P
                                                                  263170-85-0P
     263170-86-1P
                    263170-87-2P
                                                                  263170-90-7P
                                   263170-88-3P
                                                   263170-89-4P
                                   263170-93-0P
                                                                  263170-95-2P
     263170-91-8P
                    263170-92-9P
                                                   263170-94-1P
     263170-96-3P
                                   263170-98-5P
                                                   263170-99-6P
                    263170-97-4P
                                                                  263171-00-2P
                                   263171-03-5P
     263171-01-3P
                    263171-02-4P
                                                   263171-04-6P
                                                                  263171-05-7P
                    263171-07-9P
                                                   263171-09-1P
     263171-06-8P
                                   263171-08-0P
                                                                  263171-10-4P
                                   263171-13-7P
     263171-11-5P
                    263171-12-6P
                                                   263171-14-8P
                                                                  263171-15-9P
     263171-16-0P
                    263171-17-1P
                                   263171-18-2P
                                                   263171-19-3P
                                                                  263171-20-6P
                                   263171-23-9P
     263171-21-7P
                    263171-22-8P
                                                   263171-24-0P
                                                                  263171-25-1P
     263171-26-2P
                    263171-27-3P
                                   263171-28-4P
                                                   263171-29-5P
                                                                  263171-30-8P
     263171-31-9P
                                   263171-33-1P
                                                   263171-34-2P
                    263171-32-0P
                                                                  263171-35-3P
                    263171-37-5P
                                                   263171-39-7P
     263171-36-4P
                                   263171-38-6P
                                                                  263171-40-0P
```

```
263171-41-1P
                   263171-42-2P
                                  263171-43-3P
                                                263171-44-4P
                                                               263171-45-5P
    263171-46-6P
                   263171-47-7P
                                  263171-48-8P
                                                 263171-49-9P
                                                               263171-50-2P
     263171-51-3P
                                                263171-54-6P
                   263171-52-4P
                                  263171-53-5P
                                                               263171-55-7P
     263171-56-8P
                   263171-57-9P
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
    BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of 3-cyanoquinolines as protein tyrosine
       kinase inhibitors)
    142243-02-5 149433-91-0
                              150977-45-0
IT
    RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL
     (Biological study)
        (preparation of 3-cyanoquinolines as protein tyrosine
       kinase inhibitors)
IT
     59-31-4, Carbostyril
                          87-13-8, Diethyl ethoxymethylenemalonate
                                                                     91-21-4,
     1,2,3,4-Tetrahydroisoquinoline 94-05-3, Ethyl
     ethoxymethylenecyanoacetate 97-52-9, 2-Methoxy-4-nitroaniline
                                                                     99-52-5
     100-01-6, 4-Nitroaniline, reactions 103-76-4, 1-(2-
    Hydroxyethyl)piperazine 106-96-7, Propargyl bromide
                                                           107-19-7,
                       109-01-3, 1-Methylpiperazine
    Propargyl alcohol
                                                     109-86-4,
     2-Methoxyethanol 110-91-8, Morpholine, reactions 111-42-2,
    Diethanolamine, reactions 111-95-5 123-90-0, Thiomorpholine
     134-20-3, Methyl anthranilate 177-11-7, 1,4-Dioxa-8-azaspiro[4,5]decane
    350-30-1, 3-Chloro-4-fluoronitrobenzene 533-30-2, 6-Aminobenzothiazole
     536-90-3, 3-Methoxyaniline 578-66-5, 8-Aminoquinoline 580-15-4,
     6-Aminoquinoline 611-34-7, 5-Aminoquinoline 621-33-0, 3-Ethoxyaniline
     624-65-7, Propargyl chloride 632-02-0, 3-Chloropropyl p-toluenesulfonate
     645-08-9, 3-Hydroxy-4-methoxybenzoic acid 934-22-5, 5-Aminobenzimidazole
     1117-71-1, Methyl 4-bromocrotonate 1125-60-6, 5-Aminoisoquinoline
     2217-41-6, 1-Amino-5,6,7,8-tetrahydronaphthalene 2629-72-3,
     4-(3-Hydroxypropyl)pyridine 3177-80-8, 2-Amino-3-methoxybenzoic acid
     3325-11-9, 5-Aminobenzotriazole 3943-74-6, Methyl 4-hydroxy-3-
    methoxybenzoate 4442-54-0 4684-12-2, 1-Amino-4-chloronaphthalene
    4747-21-1, Isopropylmethylamine 5035-82-5, Methyl 2-amino-3,4,5-
     trimethoxybenzoate
                        5192-03-0, 5-Aminoindole
                                                  5192-23-4, 4-Aminoindole
     5318-27-4, 6-Aminoindole 5382-16-1, 4-Hydroxypiperidine
                                                               5685-05-2,
     2-Mercaptothiazole
                        6315-89-5, 4-Aminoveratrole
                                                     6967-12-0,
     6-Aminoindazole
                     7223-38-3, N,N-Dimethyl-2-propynylamine 7357-67-7,
     4-(3-Chloropropyl)morpholine 13669-62-0, 4-Chloro-6-methoxyquinoline-3-
    carbonitrile
                  14268-66-7, 3,4-Methylenedioxyaniline
                                                         19335-11-6,
     5-Aminoindazole
                     20197-71-1, Methyl 2-amino-4,5-diethoxybenzoate
     20503-40-6, 6-Amino-1,1-dioxobenzo[b]thiophene 21302-43-2,
     5-Amino-8-hydroxyquinoline dihydrochloride
                                               22013-33-8,
                                          26093-31-2, 7-Amino-4-
     6-Amino-1,4-benzodioxane 24425-40-9
                     28228-73-1, 6-Aminoindoline dihydrochloride
    methylcoumarin
                                                                  28782-50-5,
     4-Aminophthalhydrazide 29043-48-9, 5-Amino-2-methyl-1H-benzimidazole
    32770-99-3, 5-Amino-2-methylbenzothiazole dihydrochloride
                                                              38256-93-8,
    N-Methyl-2-methoxyethylamine 42533-63-1, 4-Bromomethyl-3-chloro-1-
                  50472-10-1, 2-Amino-3,6-dimethoxybenzoic acid 56354-98-4,
    nitrobenzene
     6-Amino-2-benzothiazolinone 57319-65-0, 6-Aminophthalide
                                                               57366-77-5
     61032-42-6, Methyl 2-amino-4-benzyloxy-5-methoxybenzoate
                                                              63126-47-6,
     (S)-2-Methoxymethylpyrrolidine 69975-65-1, 6-Amino-1-indanone
                  169037-24-5
                                179688-27-8, Ethyl 2-amino-4,5-bis(2-
    133303-88-5
    methoxyethoxy) benzoate
                            263171-68-2
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of 3-cyanoquinolines as protein tyrosine
       kinase inhibitors)
                2458-24-4P
                              3535-24-8P
IT
    2286-55-7P
                                         6702-50-7P, Methyl isovanillate
                                             20197-76-6P
    13280-03-0P
                 13436-14-1P
                               20197-75-5P
                                                           20629-35-0P
    26893-14-1P 27333-44-4P
                                45813-02-3P
                                             50413-49-5P
                                                           52791-03-4P
```

```
61338-35-0P
                   71083-59-5P
                                 71083-64-2P
                                               71083-71-1P
                                                              73387-74-3P
     97966-31-9P
                   111627-40-8P
                                  113290-32-7P
                                                 118764-05-9P
                                                                 198149-15-4P
                                   214470-35-6P
                                                                  214470-52-7P
     214470-27-6P
                    214470-33-4P
                                                  214470-37-8P
     214470-55-0P
                    214470-56-1P
                                   214470-57-2P
                                                  214470-58-3P
                                                                  214470-59-4P
     214470-60-7P
                    214470-61-8P
                                   214470-66-3P
                                                  214470-68-5P
                                                                  214470-72-1P
     214470-75-4P
                    214470-78-7P
                                   214470-85-6P
                                                  214470-90-3P
                                                                  214471-15-5P
     214471-46-2P
                    214471-57-5P
                                   214472-17-0P
                                                  214472-37-4P
                                                                  214472-41-0P
     214472-56-7P
                    214475-83-9P
                                   214475-85-1P
                                                  214475-98-6P
                                                                  214475-99-7P
     214476-00-3P
                    214476-04-7P
                                   214476-07-0P
                                                  214476-08-1P
                                                                  214476-09-2P
     214476-14-9P
                    214476-23-0P
                                   214476-46-7P
                                                  214476-63-8P
                                                                  214476-65-0P
     214476-68-3P
                    214476-69-4P
                                   214476-70-7P
                                                  214476-71-8P
                                                                  214476-77-4P
     214476-78-5P
                    214476-89-8P
                                   214476-99-0P
                                                  214487-27-1P
                                                                  220699-97-8P
     220699-98-9P
                    220699-99-0P
                                   220700-00-5P
                                                  220700-02-7P
                                                                  220700-03-8P
     220700-04-9P
                    220700-05-0P
                                   263148-94-3P
                                                  263148-96-5P
                                                                  263148-97-6P
     263149-09-3P
                    263149-10-6P
                                   263149-11-7P
                                                  263171-58-0P
                                                                  263171-59-1P
     263171-60-4P
                    263171-61-5P
                                   263171-62-6P
                                                  263171-63-7P
                                                                  263171-64-8P
     263171-65-9P
                    263171-66-0P
                                   263171-67-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of 3-cyanoquinolines as protein tyrosine
        kinase inhibitors)
RE.CNT
       37
              THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Anon; EP 0520722 1992 HCAPLUS
(2) Anon; EP 0566226 1993 HCAPLUS
(3) Anon; EP 0602851 1994 HCAPLUS
(4) Anon; EP 0635498 1995 HCAPLUS
(5) Anon; EP 0635507 1995 HCAPLUS
(6) Anon; WO 9515758 1995 HCAPLUS
(7) Anon; WO 9519774 1995 HCAPLUS
(8) Anon; WO 9519970 1995 HCAPLUS
(9) Anon; WO 9521613 1995 HCAPLUS
(10) Anon; WO 9523141 1995 HCAPLUS
(11) Anon; WO 9524190 1995 HCAPLUS
(12) Anon; WO 9609294 1996 HCAPLUS
(13) Anon; WO 9633977 1996 HCAPLUS
(14) Anon; WO 9633978 1996 HCAPLUS
(15) Anon; WO 9633979 1996 HCAPLUS
(16) Anon; WO 9633980 1996 HCAPLUS
(17) Anon; WO 9633981 1996 HCAPLUS
(18) Anon; WO 9802434 1998 HCAPLUS
(19) Anon; WO 9802438 1998 HCAPLUS
(20) Anon; WO 9813350 1998 HCAPLUS
(21) Anon; WO 9843960 1998 HCAPLUS
(22) Bridges, A; J Med Chem 1996, V39, P267 HCAPLUS
(23) Burke, T; Drugs Future 1992, V17, P119
(24) Chang, C; J Nat Prod 1992, V55, P1529 HCAPLUS
(25) Dolle, R; J Med Chem 1994, V372, P2627
(26) Du, J; Am J Physiol 1995, V269(2 pt 1), P487
(27) Fry, D; Science 1994, V265, P1093 HCAPLUS
(28) Gattone, V; Development Biology 1995, V169(2), P504 HCAPLUS
(29) Gazit, A; J Med Chem 1996, V35(11), P2170
(30) Ife, R; J Med Chem 1992, V35(18), P3413 HCAPLUS
(31) Maguire, M; J Med Chem 1994, V37, P2129 HCAPLUS
(32) Nauta, J; Pediatric Research 1995, V37(6), P755 HCAPLUS
(33) Rewcastle, A; J Med Chem 1996, V39, P267
(34) Spada; US 5480883 1996 HCAPLUS
(35) Traxler; US 5686457 1997 HCAPLUS
(36) Wilson, P; Eur J Cell Biol 1993, V61(1), P131 HCAPLUS
(37) Wissner; US 6002008 1999 HCAPLUS
```

RE

- L40 ANSWER 44 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2001:310060 HCAPLUS
- DN 135:74919
- ED Entered STN: 02 May 2001
- TI Molecular regulation of tumor cell vasculogenic mimicry by tyrosine phosphorylation: role of epithelial cell kinase (Eck/EphA2)
- AU Hess, Angela R.; Seftor, Elisabeth A.; Gardner, Lynn M. G.; Carles-Kinch, Kelly; Schneider, Galen B.; Seftor, Richard E. B.; Kinch, Michael S.; Hendrix, Mary J. C.
- CS Department of Anatomy and Cell Biology, University of Iowa College of Dentistry, Iowa City, IA, 52242-1109, USA
- SO Cancer Research (2001), 61(8), 3250-3255 CODEN: CNREA8; ISSN: 0008-5472
- PB American Association for Cancer Research
- DT Journal
- LA English
- CC 14-1 (Mammalian Pathological Biochemistry)
 Section cross-reference(s): 2
- AB During embryogenesis, blood vessels are formed initially by the process of vasculogenesis, the in situ differentiation of mesenchymal cells into endothelial cells, which form a primitive, patterned vasculogenic network. This is followed by angiogenesis, the sprouting of new vessels from pre-existing vasculature, to yield a more refined microcirculation. However, we and our collaborators have recently described a process termed "vasculogenic mimicry," which consists of the formation of patterned, tubular networks by aggressive melanoma tumor cells (in three-dimensional cultures in vitro), that mimics endothelial-formed vasculogenic networks and correlates with poor clin. prognosis in patients. Previous microarray anal. from our laboratory comparing the highly aggressive vs. the poorly aggressive melanoma cells revealed a significant increased expression of tyrosine kinases associated with the aggressive melanoma phenotype. Because of the important role of protein tyrosine kinases in phosphorylating various signal transduction proteins that are critical for many cellular processes (e.g., cell adhesion, migration, and invasion), we examined whether protein tyrosine kinases are involved in melanoma vasculogenic mimicry. Immunofluorescence anal. of aggressive melanoma cells forming tubular networks in vitro showed that tyrosine phosphorylation activity colocalized specifically within areas of tubular networks formation. A phosphotyrosine profile of the aggressive melanoma cells capable of forming tubular networks indicated differences in tyrosine phosphorylated proteins compared with the poorly aggressive melanoma cells (incapable of forming tubular networks). Most notably, we identified epithelial cell kinase (EphA2) as being one receptor tyrosine kinase expressed and phosphorylated exclusively in the aggressive metastatic melanoma cells. Furthermore, general inhibitors of protein tyrosine kinases hindered tube formation, and transient knockout of EphA2 abrogated the ability of tumor cells to form tubular structures. These results suggest that protein tyrosine kinases, particularly EphA2, are involved in the formation of tubular networks by aggressive melanoma tumor cells in vitro, which may represent a novel therapeutic target for further clin. investigation.
- ST **EphA2 tyrosine kinase** phosphorylation uveal melanoma angiogenesis
- IT Liver, neoplasm

```
(metastasis; Eck/EphA2 kinase in mol.
        regulation of melanoma vasculogenic mimicry by tyrosine
        phosphorylation)
IT
     Phosphorylation, biological
        (protein; Eck/EphA2 kinase in
        mol. regulation of melanoma vasculogenic mimicry by tyrosine
        phosphorylation)
IT
     Eye, neoplasm
        (uvea, melanoma, metastasis; Eck/EphA2
        kinase in mol. regulation of melanoma vasculogenic mimicry by
        tyrosine phosphorylation)
IT
     Angiogenesis
        (vasculogenic mimicry; Eck/EphA2 kinase
        in mol. regulation of melanoma vasculogenic mimicry by tyrosine
        phosphorylation)
TT
     80449-02-1, Protein tyrosine kinase
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
     effector, except adverse); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); PROC (Process)
        (Eck/EphA2 kinase in mol. regulation of
        melanoma vasculogenic mimicry by tyrosine phosphorylation)
RE.CNT
              THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bartley, T; Nature 1994, V368, P558 HCAPLUS
(2) Bissell, M; Am J Pathol 1999, V155, P675 MEDLINE
(3) Bittner, M; Nature 2000, V406, P536 HCAPLUS
(4) Burridge, K; J Cell Biol 1992, V119, P893 HCAPLUS
(5) Damsky, C; Curr Opin Cell Biol 1998, V10, P660 HCAPLUS
(6) Easty, D; Cancer Res 1995, V55, P2528 HCAPLUS
(7) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
(8) Easty, D; Int J Cancer 1999, V84, P494 HCAPLUS
(9) Easty, D; J Investig Dermatol 1993, V101, P579
(10) Folkman, J; N Engl J Med 1995, V333, P1757 MEDLINE
(11) Fox, G; Oncogene 1995, V10, P897 HCAPLUS
(12) Graham, C; Am J Pathol 1994, V145, P510 MEDLINE
(13) Khwaja, A; J Biol Chem 1998, V273, P18793 HCAPLUS
(14) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
(15) Maher, T; Histopathology 1998, V32, P217 MEDLINE
(16) Maniotis, A; Am J Pathol 1999, V155, P739 MEDLINE
(17) Miao, H; Nat Cell Biol 2000, V2, P62 HCAPLUS
(18) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS
(19) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS
(20) Pandey, A; Science 1995, V286, P567
(21) Pasquale, E; Curr Opin Cell Biol 1997, V9, P608 HCAPLUS
(22) Potter, C; Trends Genet 2000, V16, P33 HCAPLUS
(23) Rosenburg, I; Am J Physiol 1997, V273, PG824
(24) Seftor, R; Cancer Metastasis Rev 1999, V18, P359 HCAPLUS
(25) Tian, X; Development 1995, V121, P1053
(26) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
(27) Zhou, Y; J Clin Investig 1997, V99, P2139 HCAPLUS
(28) Zhou, Y; J Clin Investig 1997, V99, P2152 HCAPLUS
L40
    ANSWER 45 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2001:227357 HCAPLUS
DN
     135:3808
ED
     Entered STN: 30 Mar 2001
TI
     EphA2 overexpression causes tumorigenesis of mammary epithelial
```

```
AU
     Zelinski, Daniel P.; Zantek, Nicole Dodge; Stewart, Jane C.; Irizarry,
     Armando R.; Kinch, Michael S.
    Department of Basic Medical Sciences, Purdue University, West Lafayette,
CS
     IN, 47907-1246, USA
     Cancer Research (2001), 61(5), 2301-2306
SO
     CODEN: CNREA8; ISSN: 0008-5472
PB
    American Association for Cancer Research
DT
    Journal
LA
     English
CC
     14-1 (Mammalian Pathological Biochemistry)
     Elevated levels of protein tyrosine phosphorylation
AΒ
     contribute to a malignant phenotype, although the tyrosine
     kinases that are responsible for this signaling remain largely
     unknown. Here we report increased levels of the EphA2 (
     ECK) protein tyrosine kinase in
     clin. specimens and cell models of breast cancer. We also show that
     EphA2 overexpression is sufficient to confer malignant
     transformation and tumorigenic potential on nontransformed (MCF-10A)
    mammary epithelial cells. The transforming capacity of EphA2 is
     related to the failure of EphA2 to interact with its
     cell-attached ligands. Interestingly, stimulation of EphA2
     reverses the malignant growth and invasiveness of EphA2
     -transformed cells. Taken together, these results identify EphA2
     as a powerful oncoprotein in breast cancer.
ST
     EphA2 receptor tyrosine kinase
     mammary epithelium tumorigenesis
IT
     Phenotypes
     Signal transduction, biological
        (EphA2 overexpression causes tumorigenesis of mammary
        epithelial cells)
IT
     Ligands
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (cell-attached ligands; EphA2 overexpression causes
        tumorigenesis of mammary epithelial cells)
IT
     Mammary gland
        (epithelium; EphA2 overexpression causes tumorigenesis of
        mammary epithelial cells)
IT
     Mammary gland
        (neoplasm; EphA2 overexpression causes tumorigenesis of
        mammary epithelial cells)
IT
     Phosphorylation, biological
        (protein; EphA2 overexpression causes tumorigenesis
        of mammary epithelial cells)
IT
     Catenins
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (β-; EphA2 overexpression causes tumorigenesis of
        mammary epithelial cells)
IΤ
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);
     BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); OCCU (Occurrence); PROC (Process)
        (EphA2 overexpression causes tumorigenesis of mammary
        epithelial cells)
              THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 28
RE
```

```
(1) Bae, S; Breast Cancer Res Treat 1993, V24, P241 MEDLINE
(2) Bartley, T; Nature (Lond) 1994, V368, P558 HCAPLUS
(3) Birchmeier, W; Bioessays 1995, V17, P97 HCAPLUS
(4) Clark, G; Oncogene 1996, V12, P169 HCAPLUS
(5) Davis, S; Science (Washington DC) 1994, V266, P816 HCAPLUS
(6) Dickson, R; Endocr Rev 1995, V16, P559 HCAPLUS
(7) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
(8) Fidler, I; Cancer: Principles and Practice of Oncology 1997, P135
(9) Frisch, S; Curr Opin Cell Biol 1997, V9, P701 HCAPLUS
(10) Giunciuglio, D; Int J Cancer 1995, V63, P815 HCAPLUS
(11) Keely, P; Trends Cell Biol 1998, V8, P101 HCAPLUS
(12) Kinch, M; Hybridoma 1998, V17, P227 HCAPLUS
(13) Kinch, M; J Cell Biol 1995, V130, P461 HCAPLUS
(14) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
(15) Miao, H; Nature Cell Biol 2000, V2, P62 HCAPLUS
(16) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS
(17) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS
(18) Pauley, R; Eur J Cancer Prev 1993, V2 (Suppl 3), P67
(19) Roche, S; Curr Biol 1998, V8, P975 HCAPLUS
(20) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
(21) Ruoslahti, E; Princess Takamatsu Symp 1994, V24, P99 MEDLINE
(22) Steeg, P; Am J Pathol 1996, V149, P733 HCAPLUS
(23) Takeda, H; Oncogene 1998, V16, P3019 HCAPLUS
(24) Volberg, T; EMBO J 1992, V11, P1733 HCAPLUS
(25) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
(26) Weaver, V; Semin Cancer Biol 1995, V6, P175 HCAPLUS
(27) Weiner, L; Semin Oncol 1999, V26, P43 HCAPLUS
(28) Zantek, N; Cell Growth Differ 1999, V10, P629 HCAPLUS
L40
    ANSWER 46 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
     2001:137403 HCAPLUS
AN
     134:177365
DN
     Entered STN: 25 Feb 2001
ED
     Antibodies as a cancer diagnostic
ΤI
     Kinch, Michael Scott; Zantek, Nicole Dodge
IN
     Purdue Research Foundation, USA
PA
so
     PCT Int. Appl., 17 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM C12Q001-00
CC
     15-3 (Immunochemistry)
     Section cross-reference(s): 9, 14
FAN.CNT 1
                                          APPLICATION NO.
     PATENT NO.
                        KIND DATE
                                                                 DATE
                               -----
     -----
                        ----
                                           -----
                                                                   -----
                                           WO 2000-US22669
PΙ
     WO 2001012840
                         A2
                                20010222
                                                                   20000817 <--
                        A3
                               20010503
     WO 2001012840
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                        AA 20010222 CA 2000-2382655
A2 20020605 EP 2000-955686
     CA 2382655
                                                                   20000817 <--
     EP 1210603
                                                                   20000817 <--
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
```

```
IE, SI, LT, LV, FI, RO, MK, CY, AL
     JP 2003507023
                          T2
                                20030225
                                          JP 2001-516927
                                                                   20000817 <--
PRAI US 1999-149259P
                          P
                                19990817
                                         <--
     WO 2000-US22669
                          W
                                20000817
CLASS
 PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
                ----
 WO 2001012840 ICM
                        C120001-00
 WO 2001012840 ECLA
                        C07K016/32; G01N033/574V
     Method and kits are provided for the detection and diagnosis of metastatic
     disease. More particularly, the methods and kits employ compds. that can
     detect EphA2, a specific epithelial cell tyrosine
     kinase that is overexpressed in metastatic tumor cells. In one
     embodiment the compound is an antibody capable of binding to an epitope of
     EphA2.
ST
     EphA2 kinase antibody cancer diagnosis
IT
     Lung, neoplasm
     Neoplasm
        (antibodies as a cancer diagnostic)
IT
     Antibodies
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (antibodies as a cancer diagnostic)
IT
     Blood analysis
     Cerebrospinal fluid
     Epitopes
     Saliva
     Test kits
     Urine analysis
        (antibodies as a cancer diagnostic in relation to)
IT
     Diagnosis
        (cancer; antibodies as a cancer diagnostic)
IT
     Intestine, neoplasm
        (colon; antibodies as a cancer diagnostic)
IT
     Immunoassay
        (enzyme-linked immunosorbent assay; antibodies as a cancer diagnostic
        in relation to)
IT
     Cytometry
        (flow; antibodies as a cancer diagnostic in relation to)
IT
     Antibodies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (labeled; antibodies as a cancer diagnostic)
IT
     Mammary gland
     Prostate gland
        (neoplasm; antibodies as a cancer diagnostic)
IT
     149433-91-0, EphA2 receptor tyrosine
     kinase
     RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (antibodies as a cancer diagnostic in relation to)
IT
     21820-51-9, Phosphotyrosine
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (antibodies as a cancer diagnostic in relation to)
    ANSWER 47 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
T.40
AN
     2001:137006 HCAPLUS
DN
     134:188192
ED
     Entered STN: 25 Feb 2001
ΤI
     Treatment of metastatic disease using compounds specific for EphA2
```

```
IN
     Kinch, Michael Scott
PA
     Purdue Research Foundation, USA
SO
     PCT Int. Appl., 29 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM A61K031-00
     ICS A61K039-395; A61K049-00; C07K002-00; C07K005-00; C07K016-28
CC
     1-6 (Pharmacology)
     Section cross-reference(s): 14, 15, 63
FAN.CNT 1
                                        APPLICATION NO.
     PATENT NO.
                       KIND DATE
                                                               DATE
     -----
                               -----
                                          ------
PΙ
                              20010222 WO 2000-US22670
     WO 2001012172
                        A1
                                                               20000817 <--
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
            HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
            LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
            SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
            ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
            CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2380888
                             20010222 CA 2000-2380888
                         AA
                                                                20000817 <--
                              20020925 EP 2000-955687
     EP 1242060
                        A1
                                                               20000817 <--
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL
     JP 2003516930
                        T2
                            20030520
                                        JP 2001-516518
                                                               20000817 <--
PRAI US 1999-149258P
                        P
                              19990817
                                       <--
    WO 2000-US22670
                        W
                              20000817 <--
CLASS
              CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
               ----
WO 2001012172 ICM
                      A61K031-00
                ICS
                       A61K039-395; A61K049-00; C07K002-00; C07K005-00;
                       C07K016-28
                ECLA
WO 2001012172
                       A61K038/19; C07K016/32
AB
    The present invention is directed to compds. and methods for the treatment
    of metastatic disease. The compds. of this invention have specificity for
    EphA2, an epithelial cell tyrosine kinase that
     is overexpressed in metastatic tumor cells. The compds. used in
    accordance with this invention may be provided in a pharmaceutical composition
     for treatment of metastatic disease. For example, an EphA2
    agonist, EphrinAl-Fc (0.5 mg/mL), increased the phosphorylation
     content of EphA2 in MCFEphA2 cells. This EphA2
     stimulation reversed the effects of EphA2 overexpression.
ST
    EphA2 receptor tyrosine kinase
    antibody metastasis; cancer metastasis diagnosis treatment EphA2
    antibody
IT
    Animal cell line
        (B2D6, antibodies against; compds. specific for EphA2 for
       diagnosis and treatment of metastatic disease using compds. specific
       for)
IT
    Hybridoma
        (antibodies against; compds. specific for EphA2 for diagnosis
       and treatment of metastatic disease using compds. specific for)
IT
    Diagnosis
        (cancer, metastasis; compds. specific for EphA2 for diagnosis
       and treatment of metastatic disease using compds. specific for)
IT
    Intestine, neoplasm
```

haddad - 10 / 823259 (colon, metastasis, inhibitors; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) Antitumor agents Intestine, neoplasm (colon, metastasis; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) Drug targeting Immunotherapy Luminescence Protein sequences (compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) Growth factors, animal RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (ephrin A1-Fc; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) **Epitopes** (extracellular, of EphA2; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) Multiple myeloma (fusion with lymph node cells; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) Lymph node (fusion with myeloma cells; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific Drug delivery systems (immunoconjugates; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) Antitumor agents (lung, metastasis; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) Antitumor agents (mammary gland, metastasis; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) Lung, neoplasm Mammary gland (metastasis, inhibitors; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) Antitumor agents Lung, neoplasm (metastasis; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for)

IT

IT Antibodies

IT

ΙT

TΤ

TΤ

IT

IT

IT

IT

IT

IT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(monoclonal, conjugates, with cytotoxic agents; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for)

TT Antibodies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses) (monoclonal; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) IT Prostate gland (neoplasm, metastasis, inhibitors; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) IT Mammary gland Prostate gland (neoplasm, metastasis; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific IT Antitumor agents (prostate gland, metastasis; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific IT Phosphorylation, biological (protein; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) IT 67-43-6, Diethylenetriamine pentaacetic acid 10025-76-0, Europium trichloride RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (antibody label; compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) TT 149433-91-0, EphA2 receptor tyrosine kinase RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (compds. specific for EphA2 for diagnosis and treatment of metastatic disease using compds. specific for) RE.CNT THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Huai, J; European Journal of Neuroscience 2000, V12, P179 (2) Kinch, M; Hybridoma 1998, V17, P227 HCAPLUS (3) Lindberg, R; Molecular and Cellular Biology 1990, V10, P6316 HCAPLUS (4) Nakamoto, M; International Journal of Biochemistry & Cell Biology 1999, V32, P7 (5) Walker-Daniels, J; The Prostate 1999, V41, P275 HCAPLUS (6) Zantek, N; Cell Growth & Differentiation 1999, V10, P629 HCAPLUS L40 ANSWER 48 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN AN 2001:15481 HCAPLUS DN 134:220607 ED Entered STN: 08 Jan 2001 ΤI The ephrin-A1 ligand and its receptor, EphA2 are expressed during tumor neovascularization Ogawa, Kazushige; Pasqualini, Renata; Lindberg, Richard A.; Kain, Renate; ΑU Freeman, Andrew L.; Pasquale, Elena B. CS The Burnham Institute, La Jolla, CA, 92037, USA SO Oncogene (2000), 19(52), 6043-6052 CODEN: ONCNES; ISSN: 0950-9232 PB Nature Publishing Group DT Journal LA English CC 14-1 (Mammalian Pathological Biochemistry) Section cross-reference(s): 2 Eph receptor tyrosine kinases and AB their ephrin ligands have been implicated in embryonic vascular development and in in vivo models of angiogenesis. Rph

```
proteins may also regulate tumor neovascularization, but this role
has not been previously investigated. To screen for Eph
proteins expressed in tumor blood vessels, we used tumor
xenografts grown in nude mice from MDA-MB-435 human breast cancer cells or
KS1767 human Kaposi's sarcoma cells. By immunohistochem., the
ephrin-Al ligand and one of its receptors, EphA2
, were detected throughout tumor vasculature. Double-labeling with
anti-CD34 antibodies demonstrated that both ephrin-A1 and
EphA2 were expressed in xenograft endothelial cells and also tumor
cells. Furthermore, EphA2 was tyrosine-phosphorylated
in the xenograft tumors, indicating that it was activated, presumably by
interacting with ephrin-A1. Ephrin-A1 and
EphA2 were also detected in both the vasculature and tumor cells
of surgically removed human cancers. In an in vitro angiogenesis model, a
dominant neg. form of EphA2 inhibited capillary
tube-like formation by human umbilical vein endothelial cells (HUVECs),
demonstrating a requirement for EphA receptor
signaling. These data suggest that ephrin-Al and EphA2
play a role in human cancers, at least in part by influencing tumor
neovascularization. Eph proteins may represent
promising new targets for antiangiogenic cancer treatments.
ephrin EphA2 receptor vascular endothelium
tumor neovascularization
Sarcoma
   (Kaposi's; ephrin-Al ligand and EphA2
   receptor expression during human tumor neovascularization)
Lung, neoplasm
   (adenocarcinoma, anaplastic; ephrin-Al ligand and
   EphA2 receptor expression during human tumor
   neovascularization)
Intestine, neoplasm
   (colon, carcinoma; ephrin-A1 ligand and EphA2
   receptor expression during human tumor neovascularization)
Mammary gland
   (disease, benign; ephrin-A1 ligand and EphA2
   receptor expression during human tumor neovascularization)
Signal transduction, biological
Stomach, neoplasm
   (ephrin-A1 ligand and EphA2 receptor
   expression during human tumor neovascularization)
Growth factors, animal
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);
BSU (Biological study, unclassified); BIOL (Biological study); OCCU
(Occurrence)
   (ephrin-A1; ephrin-A1 ligand and EphA2
   receptor expression during human tumor neovascularization)
Mammary gland
   (fibroadenoma; ephrin-A1 ligand and EphA2
   receptor expression during human tumor neovascularization)
Mammary gland
   (gynecomastia; ephrin-A1 ligand and EphA2
   receptor expression during human tumor neovascularization)
Mammary gland
   (neoplasm; ephrin-Al ligand and EphA2
   receptor expression during human tumor neovascularization)
Angiogenesis
   (neovascularization; ephrin-Al ligand and EphA2
   receptor expression during human tumor neovascularization)
Kidney, neoplasm
   (renal cell carcinoma; ephrin-A1 ligand and EphA2
```

ST

IT

ΙT

```
receptor expression during human tumor neovascularization)
IT
    Lung, neoplasm
        (squamous cell carcinoma; ephrin-Al ligand and EphA2
        receptor expression during human tumor neovascularization)
IT
        (umbilical, endothelium; ephrin-A1 ligand and EphA2
        receptor expression during human tumor neovascularization)
IT
     149433-91-0, EphA2 receptor tyrosine
    RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
     effector, except adverse); BOC (Biological occurrence); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence)
        (ephrin-A1 ligand and EphA2 receptor
        expression during human tumor neovascularization)
RE.CNT
              THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Adams, R; Genes Dev 1999, V13, P295 HCAPLUS
(2) Andres, A; Oncogene 1994, V9, P1461 HCAPLUS
(3) Asahara, T; Science 1997, V275, P964 HCAPLUS
(4) Bartley, T; Nature 1994, V368, P558 HCAPLUS
(5) Baumheter, S; Science 1993, V262, P436 MEDLINE
(6) Berclaz, G; Biochem Biophys Res Commun 1996, V226, P869 HCAPLUS
(7) Bobik, A; Tumour Angiogenesis 1997, P169 HCAPLUS
(8) Brooks, P; Science 1994, V264, P569 HCAPLUS
(9) Daniel, T; Kidney Int Suppl 1996, V57, PS73 HCAPLUS
(10) Davy, A; Genes Dev 1999, V13, P3125 HCAPLUS
(11) Dodelet, V; Oncogene in press 2000
(12) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
(13) Easty, D; Int J Cancer 1999, V84, P494 HCAPLUS
(14) Eberhart, J; Dev Neurosci 2000, V22, P237 HCAPLUS
(15) Eph-Nomenclature-Committee; Cell 1997, V90, P403
(16) Flanagan, J; Annu Rev Neurosci 1998, V21, P309 HCAPLUS
(17) Flenniken, A; Dev Biol 1996, V179, P382 HCAPLUS
(18) Folkman, J; Cell 1996, V87, P1153 HCAPLUS
(19) Folkman, J; Nature Med 1995, V1, P27 HCAPLUS
(20) Fox, S; J Pathol 1995, V177, P369 MEDLINE
(21) Friedlander, M; Science 1995, V270, P1500 HCAPLUS
(22) Gale, N; Genes Dev 1999, V13, P1055 HCAPLUS
(23) Gasparini, G; Tumour Angiogenesis 1997, P29
(24) Gerety, S; Mol Cell 1999, V4, P403 HCAPLUS
(25) Hanahan, D; Cell 1996, V86, P353 HCAPLUS
(26) Hanahan, D; Science 1997, V277, P48 HCAPLUS
(27) Herndier, B; AIDS 1994, V8, P575 MEDLINE
(28) Hirai, H; Science 1987, V238, P1717 HCAPLUS
(29) Holash, J; Dev Biol 1995, V172, P683 HCAPLUS
(30) Holzman, L; Mol Cell Biol 1990, V10, P5830 HCAPLUS
(31) Huynh-Do, U; EMBO J 1999, V18, P2165 HCAPLUS
(32) Kalo, M; Cell Tissue Res 1999, V298, P1 HCAPLUS
(33) Kiyokawa, E; Cancer Res 1994, V54, P3645 HCAPLUS
(34) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
(35) Magal, E; J Neurosci Res 1996, V43, P735 HCAPLUS
(36) Maru, Y; Mol Cell Biol 1998, V8, P3770
(37) Maru, Y; Oncogene 1990, V5, P445 HCAPLUS
(38) McBride, J; Mech Dev 1998, V77, P201 HCAPLUS
(39) Mellitzer, G; Nature 1999, V400, P77 HCAPLUS
(40) Merenmies, J; Cell Growth Differ 1997, V8, P3 HCAPLUS
(41) Miao, H; Nature Cell Biol 2000, V2, P62 HCAPLUS
(42) Pandey, A; Science 1995, V268, P567 HCAPLUS
(43) Pasqualini, R; Nat Biotechnol 1997, V15, P542 HCAPLUS
```

(44) Price, J; Cancer Res 1990, V50, P717 MEDLINE

```
(45) Risau, W; Annu Rev Cell Dev Biol 1995, V11, P73 HCAPLUS
(46) Risau, W; Nature 1997, V386, P671 MEDLINE
(47) Sarma, V; J Immunol 1992, V148, P3302 HCAPLUS
(48) Sato, T; Nature 1995, V376, P70 HCAPLUS
(49) Soans, C; J Cell Biol 1996, V135, P781 HCAPLUS
(50) Soans, C; Oncogene 1994, V9, P3353 HCAPLUS
(51) Stein, E; Genes Dev 1998, V12, P667 HCAPLUS
(52) Suri, C; Cell 1996, V87, P1171 HCAPLUS
(53) Takahashi, H; Oncogene 1995, V11, P879 HCAPLUS
(54) UICC; Classification of Malignant Tumors 5th edn 1997
(55) van der Geer, P; Annu Rev Cell Biol 1994, V10, P251 HCAPLUS
(56) Walker-Daniels, J; Prostate 1999, V41, P275 HCAPLUS
(57) Wang, H; Cell 1998, V93, P741 HCAPLUS
(58) Xu, Q; Nature 1999, V399, P267 HCAPLUS
(59) Zisch, A; Oncogene 2000, V19, P177 HCAPLUS
    ANSWER 49 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2000:790501 HCAPLUS
DN
     133:350203
     Entered STN: 10 Nov 2000
ED
     Substituted 3-cyano-[1.7]-, -[1.5]-, and -[1.8]-naphthyridine
ΤI
     inhibitors of tyrosine kinases
IN
     Wissner, Allan; Hamann, Philip Ross; Yamashita, Ayako
PA
     American Cyanamid Company, USA
     PCT Int. Appl., 155 pp.
so
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM C07D471-04
     ICS A61K031-4375; A61P035-00; C07D471-04; C07D221-00; C07D221-00
CC
     28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
     Section cross-reference(s): 1
FAN.CNT 1
     PATENT NO.
                        KIND
                              DATE
                                           APPLICATION NO.
                                                                  DATE
     ------
                                            ______
                                -----
     WO 2000066583
                                20001109
                                           WO 2000-US10250
                                                                   20000418 <--
PΙ
                         A1
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                                                   20000418 <--
     CA 2365212
                          AA
                                20001109
                                          CA 2000-2365212
    BR 2000009870
                                            BR 2000-9870
                          Α
                                20020108
                                                                   20000418 <--
                                            EP 2000-926043
    EP 1171440
                          A1
                                20020116
                                                                   20000418 <--
     EP 1171440
                          B1
                                20040414
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                                            US 2000-550824
    US 6355636
                         В1
                                20020312
                                                                   20000418 <--
    JP 2002543198
                          T2
                                20021217
                                            JP 2000-615613
                                                                   20000418 <--
    NZ 514576
                          Α
                                20040227
                                            NZ 2000-514576
                                                                   20000418 <--
    AT 264328
                         Е
                                            AT 2000-926043
                                20040415
                                                                   20000418 <--
     PT 1171440
                         Т
                                20040730
                                            PT 2000-926043
                                                                   20000418 <--
    AU 776962
                        B2
                                20040930
                                            AU 2000-44639
                                                                   20000418 <--
    ES 2216884
                        Т3
                                            ES 2000-926043
                                20041101
                                                                   20000418 <--
     ZA 2001008015
                        Α
                                20030102
                                            ZA 2001-8015
                                                                   20010928 <--
    NO 2001005062
                        Α
                                20011018
                                           NO 2001-5062
                                                                   20011018 <--
```

This invention provides title compds. I [X = certain (un) substituted cycloalkyl, pyridinyl, pyrimidinyl, Ph, bicyclic aryl, or bicyclic heteroaryl; Z = NH, O, S, or NR; R = alkyl or carboalkyl; A:BD:E = (un) substituted CH:CHCH:N, CH:NCH:CH, N:CHCH:CH; n = 0-1; with numerous provisos) and their pharmaceutically acceptable salts. The compds. are inhibitors of protein tyrosine kinase , useful for treating certain cancers, polycystic kidney disease, colonic polyps, etc. A variety of example compds. and intermediates were prepared in 86 examples. For instance, 4-bromobut-2-enoyl chloride (prepared from TMS ester) was amidated with 6-amino-4-(3-bromophenylamino)-1,7naphthyridine-3-carbonitrile, and the resultant halo amide (1:1 mixture of chloro and bromo compds.) was rebrominated with NaBr and aminated with Me2NH to give title compound II. The latter compound inhibited growth of a variety of human tumor cell lines in vitro, e.g., SKBR3 with an IC50 of 0.03565 $\mu M/mL$. Inhibitions of various receptor tyrosine kinases by I were determined for selected compds. ST

cyanonaphthyridine prepn inhibitor protein

tyrosine kinase; naphthyridine cyano prepn antitumor

IT Antitumor agents

GI

AB

(bladder; preparation of substituted cyanonaphthyridine inhibitors of tyrosine kinases)

IT Intestine, neoplasm Intestine, neoplasm

```
(colon, inhibitors; preparation of substituted cyanonaphthyridine
        inhibitors of tyrosine kinases)
IT
     Intestine, neoplasm
        (colon, polyp, treatment; preparation of substituted cyanonaphthyridine
        inhibitors of tyrosine kinases)
IT
     Antitumor agents
        (colon; preparation of substituted cyanonaphthyridine inhibitors
        of tyrosine kinases)
ΙT
    Antitumor agents
        (esophagus; preparation of substituted cyanonaphthyridine inhibitors
        of tyrosine kinases)
IT
     Vascular endothelial growth factor receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
     (Miscellaneous); BIOL (Biological study); PROC (Process)
        (gene KDR, inhibitors; preparation of substituted
        cyanonaphthyridine inhibitors of tyrosine
        kinases)
IT
     Growth factor receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
     (Miscellaneous); BIOL (Biological study); PROC (Process)
        (heregulin, erbB-2, inhibitors; preparation of substituted
        cyanonaphthyridine inhibitors of tyrosine
        kinases)
IT
     Kidney, neoplasm -
     Kidney, neoplasm
     Lung, neoplasm
     Lung, neoplasm
     Ovary, neoplasm
     Ovary, neoplasm
     Stomach, neoplasm
     Stomach, neoplasm
        (inhibitors; preparation of substituted cyanonaphthyridine
        inhibitors of tyrosine kinases)
IT
     Epidermal growth factor receptors
     Vascular endothelial growth factor receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
     (Miscellaneous); BIOL (Biological study); PROC (Process)
        (inhibitors; preparation of substituted cyanonaphthyridine
        inhibitors of tyrosine kinases)
IT
     Antitumor agents
     Antitumor agents
        (kidney; preparation of substituted cyanonaphthyridine inhibitors
        of tyrosine kinases)
IT
     Antitumor agents
     Antitumor agents
        (larynx tumor inhibitors; preparation of substituted
        cyanonaphthyridine inhibitors of tyrosine
        kinases)
IT
     Antitumor agents
     Antitumor agents
        (lung; preparation of substituted cyanonaphthyridine inhibitors of
        tyrosine kinases)
IT
    Antitumor agents
        (mammary gland; preparation of substituted cyanonaphthyridine
        inhibitors of tyrosine kinases)
IT
     Antitumor agents
        (mouth; preparation of substituted cyanonaphthyridine inhibitors
        of tyrosine kinases)
     Bladder
IT
     Bladder
```

```
Esophagus
     Esophagus
     Mammary gland
     Mammary gland
    Mouth
    Mouth
        (neoplasm, inhibitors; preparation of substituted
        cyanonaphthyridine inhibitors of tyrosine
       kinases)
IT
    Antitumor agents
     Antitumor agents
        (ovary; preparation of substituted cyanonaphthyridine inhibitors
        of tyrosine kinases)
IT
    Kidney, disease
        (polycystic, treatment; preparation of substituted cyanonaphthyridine
        inhibitors of tyrosine kinases)
IT
    Antitumor agents
        (preparation of substituted cyanonaphthyridine inhibitors of
        tyrosine kinases)
IT
    Antitumor agents
    Antitumor agents
        (stomach; preparation of substituted cyanonaphthyridine inhibitors
       of tyrosine kinases)
IT
    Larynx
     Larynx
        (tumor inhibitors; preparation of substituted cyanonaphthyridine
        inhibitors of tyrosine kinases)
     305370-85-8P, 4-(3-Bromophenylamino)-6-nitro-1,8-naphthyridine-3-
TΤ
                  305370-87-0P, 6-Amino-4-(3-bromophenylamino)1,8-
     carbonitrile
     naphthyridine-3-carbonitrile 305370-90-5P, 4-(3-Chloro-4-
     fluorophenylamino) -6-nitro-1,8-naphthyridine-3-carbonitrile
     305370-92-7P, 6-Amino-4-(3-chloro-4-fluorophenylamino)-1,8-naphthyridine-3-
                   305371-19-1P, 4-(3-Bromophenylamino)-6-fluoro-1,7-
     carbonitrile
     naphthyridine-3-carbonitrile 305371-20-4P, 4-(3-Bromophenylamino)-6-(4-
     methoxybenzylamino) -1,7-naphthyridine-3-carbonitrile
                                                            305371-21-5P,
     6-Amino-4-(3-bromophenylamino)-1,7-naphthyridine-3-carbonitrile
     305371-30-6P, 6-Fluoro-4-(3-hydroxy-4-methylphenylamino)-1,7-naphthyridine-
                    305371-31-7P, 6-Fluoro-4-(4-phenoxyphenylamino)-1,7-
     3-carbonitrile
     naphthyridine-3-carbonitrile 305371-32-8P, 4-(2,4-Dichlorophenylamino)-6-
     fluoro-1,7-naphthyridine-3-carbonitrile 305371-33-9P,
     4-(3-Chloro-4-fluorophenylamino)-6-fluoro-1,7-naphthyridine-3-carbonitrile
     305371-34-0P, 4-(4-Chloro-2-fluorophenylamino)-6-fluoro-1,7-naphthyridine-
     3-carbonitrile
                     305371-47-5P, 4-(3-Bromophenylamino)-6-
     (trimethylsilanylethynyl)-1,7-naphthyridine-3-carbonitrile
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (drug candidate; preparation of substituted cyanonaphthyridine
        inhibitors of tyrosine kinases)
TΤ
     305370-86-9P, 4-(3-Bromophenylamino)-6-nitro-1,8-naphthyridine-3-
     carbonitrile hydrochloride
                                 305370-88-1P, N-[5-(3-Bromophenylamino)-6-
     cyano-1,8-naphthyridin-3-yl]acrylamide 305370-89-2P, But-2-ynoic acid
     [5-(3-bromophenylamino)-6-cyano-1,8-naphthyridin-3-yl]amide
     305370-91-6P, 4-(3-Chloro-4-fluorophenylamino)-6-nitro-1,8-naphthyridine-3-
     carbonitrile hydrochloride 305370-93-8P, But-2-ynoic acid
     [5-(3-chloro-4-fluorophenylamino)-6-cyano-1,8-naphthyridin-3-yl]amide
     305370-94-9P, N-[5-(3-Bromophenylamino)-6-cyano-1,8-naphthyridin-3-yl]-2-
     chloroacetamide
                      305370-95-0P, 4-(Dimethylamino)but-2-enoic acid
     [5-(3-bromophenylamino)-6-cyano-1,8-naphthyridin-3-yl]amide
```

```
305370-99-4P, 4-(3-Bromophenylamino)-6-ethoxy-1,5-naphthyridine-3-
               305371-01-1P, 4-(3-Bromophenylamino)-1,5-naphthyridine-3-
carbonitrile
               305371-08-8P, 4-(3-Hydroxy-4-methylphenylamino)-6-(3-
carbonitrile
morpholin-4-ylpropoxy)-1,5-naphthyridine-3-carbonitrile
                                                          305371-09-9P,
4-(3-Bromophenylamino)-6-(3-morpholin-4-ylpropoxy)-1,5-naphthyridine-3-
              305371-10-2P, 4-(3-Hydroxy-4-methylphenylamino)-6-(2-
carbonitrile
morpholin-4-ylethoxy)-1,5-naphthyridine-3-carbonitrile
                                                         305371-11-3P,
4-(3-Bromophenylamino)-6-(2-morpholin-4-ylethoxy)-1,5-naphthyridine-3-
carbonitrile
              305371-14-6P, 6-Amino-4-(3-bromophenylamino)-1,5-
naphthyridine-3-carbonitrile
                              305371-23-7P, But-2-ynoic acid
[4-(3-bromophenylamino)-3-cyano-1,7-naphthyridin-6-yl]amide
305371-24-8P, 4-Dimethylaminobut-2-enoic acid [4-(3-bromophenylamino)-3-
cyano-1,7-naphthyridin-6-yl]amide 305371-27-1P, 4-(3-Bromophenylamino)-6-
(2-morpholin-4-ylethylamino)1,7-naphthyridine-3-carbonitrile
305371-28-2P, 4-(3-Bromophenylamino)-6-methylamino-1,7-naphthyridine-3-
              305371-29-3P, 1-[4-(3-Bromophenylamino)-3-cyano-1,7-
carbonitrile
naphthyridin-6-yl]-4-dimethylaminopyridinium fluoride
                                                       305371-35-1P,
4-(4-Chloro-2-fluorophenoxy)-6-fluoro-1,7-naphthyridine-3-carbonitrile
305371-36-2P, 6-(2-Dimethylaminoethoxy)-4-(4-phenoxyphenylamino)-1,7-
naphthyridine-3-carbonitrile
                             305371-37-3P, 4-(3-Chloro-4-
fluorophenylamino) -6-(2-dimethylaminoethoxy) -1,7-naphthyridine-3-
              305371-38-4P, 4-(2,4-Dichlorophenylamino)-6-(2-
carbonitrile
dimethylaminoethoxy) -1,7-naphthyridine-3-carbonitrile
                                                        305371-39-5P,
4-(4-Chloro-2-fluorophenylamino)-6-(2-dimethylaminoethoxy)-1,7-
naphthyridine-3-carbonitrile
                              305371-40-8P, 4-(3-Bromophenylamino)-6-(2-
dimethylaminoethoxy) -1,7-naphthyridine-3-carbonitrile
                                                        305371-41-9P,
6-(2-Dimethylaminoethoxy)-4-(3-hydroxy-4-methylphenylamino)-1,7-
naphthyridine-3-carbonitrile 305371-44-2P, 4-(3-Bromophenylamino)-6-
chloro-1,7-naphthyridine-3-carbonitrile
                                        305371-49-7P,
4-(3-Bromophenylamino)-6-ethynyl-1,7-naphthyridine-3-carbonitrile
305371-50-0P, 1-[4-(3-Bromophenylamino)-3-cyano-1,7-naphthyridin-6-yl]-4-
dimethylaminopyridinium
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
   (drug candidate; preparation of substituted cyanonaphthyridine
   inhibitors of tyrosine kinases)
79079-06-4, Epidermal Growth Factor Receptor Kinase
80449-02-1, Protein tyrosine kinase
142243-02-5, Mitogen Activated Protein Kinase
142805-58-1, MAPK kinase 149433-91-0, ECK
kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
(Miscellaneous); BIOL (Biological study); PROC (Process)
   (inhibitors; preparation of substituted cyanonaphthyridine
   inhibitors of tyrosine kinases)
456-24-6P, 2-Fluoro-5-nitropyridine
                                      1827-27-6P, 6-Fluoropyridin-3-
         4441-30-9P, 3-Morpholinopropanol 5350-93-6P,
                           13280-03-0P, 4-Chlorobut-2-ynoic acid
6-Chloropyridin-3-ylamine
20629-35-0P, 4-Bromocrotonic acid
                                  31594-45-3P, 2-Ethoxy-5-nitropyridine
37616-36-7P, Sodium(2-dimethylaminoethoxide)
                                             45813-02-3P,
1-Methyl-4-prop-2-ynylpiperazine 51544-74-2P, 4-Bromo-2-butenoyl
chloride
           52025-34-0P, 2-Ethoxy-5-aminopyridine 118764-05-9P,
4-Dimethylaminobut-2-ynoic acid 171178-41-9P, (6-Fluoropyridin-3-
yl)carbamic acid tert-butyl ester 171178-42-0P, 5-tert-
Butoxycarbonylamino-2-fluoroisonicotinic acid
                                              171178-45-3P,
(6-Chloropyridin-3-yl)carbamic acid tert-butyl ester
                                                       171178-46-4P,
5-tert-Butoxycarbonylamino-2-chloroisonicotinic acid
                                                       198149-15-4P,
(2S) -2- (Methoxymethyl) -1-prop-2-ynylpyrrolidine
                                                  214487-27-1P,
4-(4-Methylpiperazin-1-yl)but-2-ynoic acid
                                            220699-97-8P,
```

IT

IT

```
Bis (2-methoxyethyl) (prop-2-ynyl) amine
                                        220699-98-9P, 4-[Bis(2-
methoxyethyl)amino]but-2-ynoic acid 220699-99-0P, (2-
Methoxyethyl) methylprop-2-ynylamine
                                    220700-00-5P, 4-[N-(2-Methoxyethyl)-
N-methylamino]but-2-ynoic acid
                                 220700-02-7P
                                                220700-03-8P,
4-(Allylmethylamino)but-2-ynoic acid
                                       220700-04-9P, 4-(2-
Methoxyethoxy)but-2-ynoic acid
                                 220700-05-0P, 4-(Methoxymethoxy)but-2-
ynoic acid
             263148-94-3P, 4-[(2S)-2-(Methoxymethyl)pyrrolidin-1-yl]but-2-
ynoic acid
             263148-96-5P, 4-(1,4-Dioxa-8-azaspiro[4.5]dec-8-yl)but-2-
            263148-97-6P, 3-(1,4-Dioxa-8-azaspiro[4.5]dec-8-yl)prop-1-yne
ynoic acid
305370-82-5P, 2-(2-Chloro-5-nitropyridine-3-carbonyl)-3-
(dimethylamino)acrylonitrile 305370-83-6P, 6-Nitro-4-oxo-1,4-dihydro-1,8-
                               305370-84-7P, 4-Chloro-6-nitro-1,8-
naphthyridine-3-carbonitrile
naphthyridine-3-carbonitrile 305370-96-1P, 2-Cyano-3-(6-ethoxypyridin-3-
                                   305370-97-2P, 6-Ethoxy-4-hydroxy-1,5-
ylamino) acrylic acid ethyl ester
naphthyridine-3-carbonitrile 305370-98-3P, 4-Chloro-6-ethoxy-1,5-
                               305371-00-0P, 4-Hydroxy-1,5-naphthyridine-3-
naphthyridine-3-carbonitrile
carbonitrile
              305371-02-2P, 4-Chloro-1,5-naphthyridine-3-carbonitrile
305371-03-3P, 2-(3-Morpholin-4-ylpropoxy)-5-nitropyridine 305371-04-4P,
2-Cyano-3-[[6-(3-morpholin-4-ylpropoxy)pyridin-3-yl}amino]acrylic acid
              305371-05-5P, 2-(3-Morpholin-4-ylpropoxy)-5-aminopyridine
ethyl ester
305371-06-6P, 4-Hydroxy-6-(3-morpholin-4-ylpropoxy)-1,5-naphthyridine-3-
              305371-07-7P, 4-Chloro-6-(3-morpholin-4-ylpropoxy)-1,5-
carbonitrile
naphthyridine-3-carbonitrile
                               305371-12-4P, 6-Acetamido-4-hydroxy-1,5-
naphthyridine-3-carbonitrile 305371-13-5P, 6-Acetamido-4-chloro-1,5-
naphthyridine-3-carbonitrile 305371-15-7P, 5-tert-Butoxycarbonylamino-2-
fluoroisonicotinic acid methyl ester
                                      305371-16-8P, [6-Fluoro-4-(3-
nitrilopropionyl)pyridin-3-yl]carbamic acid tert-butyl ester
305371-17-9P, 6-Fluoro-4-hydroxy-1,7-naphthyridine-3-carbonitrile
305371-18-0P, 4-Chloro-6-fluoro-1,7-naphthyridine-3-carbonitrile
305371-22-6P, 6-Amino-4-(4-methoxybenzylamino)-1,7-naphthyridine-3-
carbonitrile
             305371-25-9P, 4-Bromobut-2-enoic acid [4-(3-
bromophenylamino) -3-cyano-1,7-naphthyridin-6-yl]amide
                                                        305371-26-0P,
4-Chlorobut-2-enoic acid [4-(3-bromophenylamino)-3-cyano-1,7-naphthyridin-
            305371-42-0P, 5-tert-Butoxycarbonylamino-2-chloroisonicotinic
6-yl]amide
                    305371-43-1P, 6-Chloro-4-hydroxy-1,7-naphthyridine-3-
acid methyl ester
carbonitrile
               305371-45-3P, 4,6-Dichloro-1,7-naphthyridine-3-carbonitrile
305371-46-4P, 4-Hydroxy-6-(trimethylsilanylethynyl)-1,7-naphthyridine-3-
carbonitrile
              305371-48-6P, 4-Chloro-6-trimethylsilanylethynyl-1,7-
naphthyridine-3-carbonitrile
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
   (intermediate; preparation of substituted cyanonaphthyridine
   inhibitors of tyrosine kinases)
75-05-8, Acetonitrile, reactions
                                   79-04-9, Chloroacetyl chloride
94-05-3, Ethyl(ethoxymethylene)cyanoacetate 106-96-7, Propargyl bromide
107-19-7, Propargyl alcohol 107-30-2, Chloromethyl methyl ether
108-01-0, 2-Dimethylaminoethanol
                                   109-01-3, 1-Methylpiperazine
109-86-4, 2-Methoxyethanol
                             110-91-8, Morpholine, reactions
                                                               111-95-5
139-59-3, 4-Phenoxyaniline
                             177-11-7, 1,4-Dioxa-8-azaspiro[4.5]decane
348-62-9, 4-Chloro-2-fluorophenol 367-21-5, 3-Chloro-4-fluoroaniline
462-08-8, 3-Aminopyridine 554-00-7, 2,4-Dichloroaniline 590-93-2, 2-Butynoic acid 591-19-5, 3-Bromoaniline 622-40-2, 2-Morpholinoethanol
                                        627-37-2, Allylmethylamine
624-65-7, Propargyl chloride
                              627-18-9
                              1066-54-2, Trimethylsilanylethyne
814-68-6, Acryloyl chloride
1117-71-1, Methyl 4-bromocrotonate 1122-58-3, 4-Dimethylaminopyridine
2038-03-1, N-(2-Aminoethyl)morpholine
                                       2393-23-9, 4-Methoxybenzylamine
2407-68-3, 3-Dimethylaminoacrylonitrile 2835-95-2, 3-Hydroxy-4-
methylaniline
               4214-76-0, 2-Amino-5-nitropyridine
                                                     4548-45-2,
2-Chloro-5-nitropyridine 4637-24-5, Dimethylformamide dimethyl acetal
7223-38-3, 1-Dimethylamino-2-propyne
                                     24424-99-5, Di-tert-butyl
```

IT

RE

AN

DN

ED

TТ

ΔIJ

CS

SO

PΒ

DT

LA

CC

ΔR

ST

IT

IT

TT

TT

```
38256-93-8, N-(2-Methoxyethyl) methylamine 42959-38-6,
     3-Carboxy-2-chloro-5-nitropyridine 57946-56-2, 4-Chloro-2-fluoroaniline
     63126-47-6, (S)-2-(Methoxymethyl)pyrrolidine 79863-92-6, Trimethylsilyl
     4-bromo-2-butenoate
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (starting material; preparation of substituted cyanonaphthyridine
        inhibitors of tyrosine kinases)
              THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
(1) American Cyanamid Co; WO 9843960 A 1998 HCAPLUS
(2) Zeneca; WO 9813350 A 1998 HCAPLUS
L40 ANSWER 50 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
    2000:108659 HCAPLUS
     132:234707
    Entered STN: 16 Feb 2000
    Activation of EphA2 kinase suppresses integrin
     function and causes focal-adhesion-kinase dephosphorylation
    Miao, Hui; Burnett, Elisabeth; Kinch, Michael; Simon, Erin;
     Wang, Bingcheng
    Rammelkamp Center for Research, MetroHealth Campus, Case Western Reserve
    University School of Medicine, Cleveland, OH, 44109, USA
    Nature Cell Biology (2000), 2(2), 62-69
     CODEN: NCBIFN; ISSN: 1465-7392
    Macmillan Magazines Ltd
    Journal
    English
     13-2 (Mammalian Biochemistry)
     Interactions between receptor tyrosine kinases
    of the Eph family and their ligands, ephrins, are
     implicated in establishment of organ boundaries and repulsive guidance of
     cell migration during development, but the mechanisms by which this is
     achieved are unclear. Here we show that activation of endogenous
     EphA2 kinase induces an inactive conformation of
     integrins and inhibits cell spreading, migration and integrin-mediated
     adhesion. Moreover, EphA2 is constitutively associated with
     focal-adhesion kinase (FAK) in resting cells. Within one minute
     after stimulation of EphA2 with its ligand, ephrin-A1,
     the protein tyrosine phosphatase SHP2 is recruited to
     EphA2; this is followed by dephosphorylation of FAK and paxillin,
     and dissociation of the FAK-EphA2 complex. We conclude that
     Eph kinases mediate some of their functions by neg.
     regulating integrins and FAK.
     EphA2 FAK kinase dephosphorylation ephrinA1
     integrin cell migration adhesion
     Integrins
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (activation of EphA2 kinase suppresses integrin
        function and causes focal-adhesion-kinase dephosphorylation)
     Cell adhesion
     Cell migration
        (activation of EphA2 kinase suppresses integrin
        function and inhibits)
     Spreading
        (biol.; activation of EphA2 kinase suppresses
        integrin function and inhibits)
    Proteins, specific or class
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
```

```
(ephrin-A1; activation of EphA2 kinase
        suppresses integrin function and causes focal-adhesion-kinase
        dephosphorylation)
IT
    Phosphorylation, biological
        (protein; activation of EphA2 kinase
        suppresses integrin function and causes focal-adhesion-kinase
        dephosphorylation)
     144114-16-9, Focal adhesion kinase
IT
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (complex with EphA2 kinase; activation of
        EphA2 kinase suppresses integrin function and causes
        focal-adhesion-kinase dephosphorylation)
IT
    149433-91-0, EphA2 receptor tyrosine
    kinase
    RL: BAC (Biological activity or effector, except adverse); BPR (Biological
    process); BSU (Biological study, unclassified); BIOL (Biological study);
     PROC (Process)
        (complex with focal adhesion kinase; activation of
        EphA2 kinase suppresses integrin function and causes
        focal-adhesion-kinase dephosphorylation)
RE.CNT
              THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Calalb, M; Mol Cell Biol 1995, V15, P954 HCAPLUS
(2) Cary, L; J Cell Sci 1996, V109, P1787 HCAPLUS
(3) Cirri, P; J Biol Chem 1998, V273, P32522 HCAPLUS
(4) Davis, S; Science 1994, V266, P816 HCAPLUS
(5) Defilippi, P; Exp Cell Res 1995, V221, P141 HCAPLUS
(6) Drescher, U; Cell 1995, V82, P359 HCAPLUS
(7) Eph Nomenclature Committe; Cell 1997, V90, P403
(8) Faull, R; J Cell Biol 1993, V121, P155 HCAPLUS
(9) Flenniken, A; Dev Biol 1996, V179, P382 HCAPLUS
(10) Gailit, J; J Biol Chem 1988, V263, P12927 HCAPLUS
(11) Gale, N; Cell Tissue Res 1997, V290, P227 HCAPLUS
(12) Gale, N; Neuron 1996, V17, P9 HCAPLUS
(13) Gilmore, A; Mol Biol Cell 1996, V7, P1209 HCAPLUS
(14) Guan, J; Nature 1992, V358, P690 HCAPLUS
(15) Hock, B; Proc Natl Acad Sci 1998, V95, P9779 HCAPLUS
(16) Holland, S; EMBO J 1997, V16, P3877 HCAPLUS
(17) Huynh-Do, U; EMBO J 1999, V18, P2165 HCAPLUS
(18) Hynes, R; Cell 1987, V48, P549 HCAPLUS
(19) Krull, C; Curr Biol 1997, V7, P571 HCAPLUS
(20) Lauffenburger, D; Cell 1996, V84, P359 HCAPLUS
(21) Lemmon, V; Neuron 1989, V2, P1597 HCAPLUS
(22) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
(23) Meima, L; Eur J Neurosci 1997, V9, P177 MEDLINE
(24) Meima, L; Mol Cell Neurosci 1997, V9, P314 HCAPLUS
(25) Mellitzer, G; Nature 1999, V400, P77 HCAPLUS
(26) Neel, B; Curr Opin Cell Biol 1997, V9, P193 HCAPLUS
(27) O'Toole, T; J Cell Biol 1994, V124, P1047 HCAPLUS
(28) Pandey, A; Curr Biol 1995, V5, P986 HCAPLUS
(29) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS
(30) Retta, S; Exp Cell Res 1996, V229, P307 HCAPLUS
(31) Richardson, A; Bioessays 1995, V17, P229 HCAPLUS
(32) Richardson, A; Mol Cell Biol 1997, V17, P6906 HCAPLUS
(33) Richardson, A; Nature 1996, V380, P538 HCAPLUS
(34) Romer, L; Mol Biol Cell 1994, V5, P349 HCAPLUS
(35) Schaller, M; J Cell Biol 1995, V130, P1181 HCAPLUS
(36) Schaller, M; Mol Cell Biol 1995, V15, P2635 MEDLINE
(37) Schlaepfer, D; Trends Cell Biol 1998, V8, P151 HCAPLUS
```

```
(38) Schwartz, M; Annu Rev Cell Dev Biol 1995, V11, P549 HCAPLUS
(39) Smith, A; Curr Biol 1997, V7, P561 HCAPLUS
(40) Stein, E; Genes Dev 1998, V12, P667 HCAPLUS
(41) Stein, E; J Biol Chem 1996, V271, P23588 HCAPLUS
(42) Tonks, N; Cell 1996, V87, P365 HCAPLUS
(43) Torres, R; Neuron 1998, V21, P1453 HCAPLUS
(44) van de Wiel-van Kemenade, E; J Cell Biol 1992, V117, P461 HCAPLUS
(45) Wang, H; Cell 1998, V93, P741 HCAPLUS
(46) Wang, H; Neuron 1997, V18, P383 HCAPLUS
(47) Xu, Q; Nature 1999, V399, P267 HCAPLUS
(48) Yamauchi, K; J Biol Chem 1995, V270, P17716 HCAPLUS
(49) Zisch, A; Oncogene 1998, V16, P2657 HCAPLUS
L40 ANSWER 51 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     1999:811742 HCAPLUS
DN
     132:235140
ED
     Entered STN: 26 Dec 1999
     Overexpression of the EphA2 tyrosine kinase
TI
     in prostate cancer
AU
     Walker-Daniels, J.; Coffman, K.; Azimi, M.; Rhim, J. S.; Bostwick, D. G.;
     Snyder, P.; Kerns, B. J.; Waters, D. J.; Kinch, M. S.
CS
     Department of Basic Medical Sciences, Purdue University, West Lafayette,
     IN, USA
SO
     Prostate (New York) (1999), 41(4), 275-280
     CODEN: PRSTDS; ISSN: 0270-4137
PΒ
     Wiley-Liss, Inc.
DT
     Journal
LA
     English
CC
     14-1 (Mammalian Pathological Biochemistry)
AB
     BACKGROUND. Mols. that are highly expressed by human prostate cancers may
     serve as therapeutically relevant targets or tumor markers.
     Tyrosine kinases are frequently over-expressed in
     metastatic tumor cells and this prompted us to screen for tyrosine
     kinases that are overexpressed in prostate cancer cells. METHODS.
     Expression levels of the EphA2 receptor
     tyrosine kinase were determined by Western blot anal. in
     canine and human prostate cancer cell lines and in immortalized and
     transformed variants of 267B1 prostatic epithelial cells. EphA2
     levels in benign human prostate and prostate cancers were also determined in
     formalin-fixed, paraffin-embedded tissues using immunohistochem. staining.
     RESULTS. Metastatic prostate cancer cells overexpressed EphA2 by
     10-100 fold as compared with non-invasive prostatic epithelial cells.
     EphA2 immunoreactivity in vivo was also significantly greater in
     human prostate cancers as compared with benign prostate epithelium.
     CONCLUSIONS. The EphA2 receptor tyrosine
     kinase is differentially expressed in human and canine prostate
     cancer cell lines and overexpressed in human prostate cancers as compared
     with benign prostate tissues. Metastasis-derived canine prostate
     carcinoma cell lines overexpress EphA2 and may provide pre-clin.
     models to further evaluate the role of EphA2 in prostate
     carcinogenesis. Further investigations are needed to determine the utility of
     EphA2 as a tumor marker and a novel target in human prostate
     cancer.
ST
     EphA2 tyrosine kinase prostate cancer
IT
    Diagnosis
        (cancer; overexpression of the EphA2 tyrosine
        kinase in canine and human prostate cancer cells)
IT
     Prostate gland
        (neoplasm, metastasis; overexpression of the EphA2
        tyrosine kinase in canine and human prostate cancer
```

```
cells)
```

IT Prostate gland

(neoplasm; overexpression of the EphA2 tyrosine

kinase in canine and human prostate cancer cells)

IT Dog (Canis familiaris)

Tumor markers

(overexpression of the EphA2 tyrosine

kinase in canine and human prostate cancer cells)

IT 149433-91-0, EphA2 receptor tyrosine

kinase

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses) (overexpression of the EphA2 tyrosine

kinase in canine and human prostate cancer cells)

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Andres, A; Oncogene 1994, V9, P1461 HCAPLUS
- (2) Baselga, J; Cancer Res 1998, V58, P2825 HCAPLUS
- (3) Easty, D; Int J Cancer 1995, V60, P129 HCAPLUS
- (4) Gale, N; Cell Tissue Res 1997, V290, P227 HCAPLUS
- (5) Grasso, A; Oncogene 1997, V15, P2705 HCAPLUS
- (6) Kinch, M; Hybridoma 1998, V17, P227 HCAPLUS
- (7) Kinch, M; J Cell Biol 1995, V130, P461 HCAPLUS
- (8) Kondapaka, B; Mol Cell Endocrinol 1996, V117, P53 HCAPLUS
- (9) Kuettel, M; Cancer Res 1996, V56, P5 HCAPLUS
- (10) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
- (11) Nemoto, T; Pathobiology 1997, V65, P195 HCAPLUS
- (12) Pandey, A; Curr Biol 1995, V5, P986 HCAPLUS
- (13) Parda, D; Prostate 1993, V23, P91 HCAPLUS
- (14) Pasquale, E; Curr Opin Cell Biol 1997, V9, P608 HCAPLUS
- (15) Patarca, R; Crit Rev Oncogenesis 1996, V7, P5
- (16) Press, M; Prog Clin Biol Res 1990, V354A, P209 MEDLINE
- (17) Rhim, J; Crit Rev Oncogenesis 1997, V8, P305 HCAPLUS
- (18) Robinson, D; Proc Natl Acad Sci 1996, V93, P5958 HCAPLUS
- (19) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
- (20) Tremblay, L; Int J Cancer 1996, V68, P164 HCAPLUS
- (21) Visakorpi, T; Mod Pathol 1992, V5, P643 MEDLINE
 (22) Webber, M; Prostate 1997, V30, P58 HCAPLUS
- (23) Witte, O; Cancer Res 1993, V53, P485 HCAPLUS
- L40 ANSWER 52 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 1999:639316 HCAPLUS
- DN 131:334871
- ED Entered STN: 08 Oct 1999
- TI E-cadherin regulates the function of the EphA2 receptor tyrosine kinase
- AU Zantek, Nicole Dodge; Azimi, Minoudokht; Fedor-Chaiken, Mary; Wang, Bingcheng; Brackenbury, Robert; Kinch, Michael S.
- CS Department of Basic Medical Sciences and Purdue Cancer Center, Purdue University, West Lafayette, IN, 47907, USA
- SO Cell Growth & Differentiation (1999), 10(9), 629-638 CODEN: CGDIE7; ISSN: 1044-9523
- PB American Association for Cancer Research
- DT Journal
- LA English
- CC 13-2 (Mammalian Biochemistry)
 Section cross-reference(s): 14
- AB EphA2 is a member of the Eph family of receptor tyrosine kinases, which are increasingly understood to play critical roles in disease and development.

We report here the regulation of EphA2 by E-cadherin. In nonneoplastic epithelia, EphA2 was tyrosine -phosphorylated and localized to sites of cell-cell contact. These properties required the proper expression and functioning of E-cadherin. In breast cancer cells that lack E-cadherin, the phosphotyrosine content of EphA2 was decreased, and EphA2 was redistributed into membrane ruffles. Expression of E-cadherin in metastatic cells restored a more normal pattern of EphA2 phosphorylation and localization. Activation of EphA2, either by E-cadherin expression or antibody-mediated aggregation, decreased cell-extracellular matrix adhesion and cell growth. Altogether, this demonstrates that EphA2 function is dependent on E-cadherin and suggests that loss of E-cadherin function may alter neoplastic cell growth and adhesion via effects on EphA2. EphA2 receptor tyrosine kinase localization phosphorylation E cadherin; mammary gland epithelium breast cancer metastasis EphA2 E cadherin; cell adhesion proliferation cancer metastasis EphA2 E cadherin Cadherins RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (E-; localization and phosphorylation of EphA2 receptor tyrosine kinase is dependent on E-cadherin and evidence that loss of E-cadherin function may alter neoplastic cell growth and adhesion via effects on EphA2) Cell junction (EphA2 at; localization and phosphorylation of EphA2 receptor tyrosine kinase is dependent on E-cadherin and evidence that loss of E-cadherin function may alter neoplastic cell growth and adhesion via effects on EphA2) Mammary gland (epithelium, EphA2 in; localization and phosphorylation of EphA2 receptor tyrosine kinase is dependent on E-cadherin and evidence that loss of E-cadherin function may alter neoplastic cell growth and adhesion via effects on EphA2) Cell junction (focal contact; localization and phosphorylation of EphA2 receptor tyrosine kinase is dependent on E-cadherin and evidence that loss of E-cadherin function may alter neoplastic cell growth and adhesion via effects on EphA2) Cell adhesion Cell proliferation (localization and phosphorylation of EphA2 receptor tyrosine kinase is dependent on E-cadherin and evidence that loss of E-cadherin function may alter neoplastic cell growth and adhesion via effects on EphA2) Organelle (membrane ruffles, EphA2 in; localization and phosphorylation of EphA2 receptor tyrosine kinase is dependent on E-cadherin and evidence that loss of E-cadherin function may alter neoplastic cell growth and adhesion via effects on EphA2) Mammary gland (neoplasm, EphA2 in; localization and phosphorylation of EphA2 receptor tyrosine kinase is dependent on E-cadherin and evidence that loss of E-cadherin function may alter neoplastic cell growth and adhesion via effects on

ST

TΤ

TΤ

IT

IT

TT

IT

IT

EphA2)

```
IT
    Mammary gland
        (neoplasm, metastasis, EphA2 in relation to; localization and
        phosphorylation of EphA2 receptor tyrosine
        kinase is dependent on E-cadherin and evidence that loss of
        E-cadherin function may alter neoplastic cell growth and adhesion via
        effects on EphA2)
IT
    Phosphorylation, biological
        (protein, tyrosine; localization and
        phosphorylation of EphA2 receptor tyrosine
        kinase is dependent on E-cadherin and evidence that loss of
        E-cadherin function may alter neoplastic cell growth and adhesion via
        effects on EphA2)
IT
    Cell membrane
        (ruffles, EphA2 in; localization and phosphorylation of
        EphA2 receptor tyrosine kinase is
        dependent on E-cadherin and evidence that loss of E-cadherin function
        may alter neoplastic cell growth and adhesion via effects on
        EphA2)
T.T
     149433-91-0, EphA2 receptor tyrosine
    kinase
    RL: BAC (Biological activity or effector, except adverse); BOC (Biological
     occurrence); BPR (Biological process); BSU (Biological study,
     unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
        (localization and phosphorylation of EphA2 receptor
        tyrosine kinase is dependent on E-cadherin and
        evidence that loss of E-cadherin function may alter neoplastic cell
        growth and adhesion via effects on EphA2)
             THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
        60
RE
(1) Andres, A; Int J Cancer 1995, V63, P288 HCAPLUS
(2) Bae, S; Breast Cancer Res Treat 1993, V24, P241 MEDLINE
(3) Behrens, J; Cancer Treat Res 1994, V71, P251 MEDLINE
(4) Behrens, J; J Cell Biol 1993, V120, P757 HCAPLUS
(5) Burridge, K; Annu Rev Cell Biol 1988, V4, P487 HCAPLUS
(6) Burridge, K; Annu Rev Cell Dev Biol 1996, V12, P463 HCAPLUS
(7) Cance, W; Breast Cancer Res Treat 1995, V35, P105 HCAPLUS
(8) Chen, H; J Cell Sci 1997, V110, P345 HCAPLUS
(9) Easty, D; Cancer Res 1995, V55, P2528 HCAPLUS
(10) Fagotto, F; Dev Biol 1996, V180, P445 HCAPLUS
(11) Foulkes, J; J Biol Chem 1985, V260, P8070 HCAPLUS
(12) Frixen, U; J Cell Biol 1991, V113, P173 HCAPLUS
(13) Gale, N; Cell Tissue Res 1997, V290, P227 HCAPLUS
(14) Gale, N; Neuron 1996, V17, P9 HCAPLUS
(15) Geiger, B; Annu Rev Cell Biol 1992, V8, P307 HCAPLUS
(16) George, S; Cell 1998, V92, P633 HCAPLUS
(17) Hamaguchi, M; EMBO J 1993, V12, P307 HCAPLUS
(18) Henkemeyer, M; Cell 1996, V86, P35 HCAPLUS
(19) Holland, S; EMBO J 1997, V16, P3877 HCAPLUS
(20) Hutchcroft, J; J Biol Chem 1991, V266, P14846 HCAPLUS
(21) Kandikonda, S; Cell Adhes Commun 1996, V4, P13 HCAPLUS
(22) Kinch, M; Biochem Soc Trans 1995, V23, P446 HCAPLUS
(23) Kinch, M; Cell Adhes Commun 1997, V4, P425 HCAPLUS
(24) Kinch, M; Hybridoma 1998, V17, P227 HCAPLUS
(25) Kinch, M; J Cell Biol 1995, V130, P461 HCAPLUS
(26) Kopreski, M; Anticancer Res 1996, V16, P3037 MEDLINE
(27) Lindberg, R; Mol Cell Biol 1990, V10, P6316 HCAPLUS
(28) Lower, E; Breast Cancer Res Treat 1993, V26, P217 MEDLINE
(29) Magal, E; J Neurosci Res 1996, V43, P735 HCAPLUS
(30) Maher, P; Proc Natl Acad Sci USA 1985, V82, P6576 HCAPLUS
(31) Marrs, J; J Cell Biol 1995, V129, P507 HCAPLUS
```

```
(32) Maru, Y; Oncogene 1990, V5, P445 HCAPLUS
(33) Matsuyoshi, N; J Cell Biol 1992, V118, P703 HCAPLUS
(34) Murphy, L; Cancer Res 1988, V48, P4555 HCAPLUS
(35) Nose, A; Cell 1988, V54, P993 HCAPLUS
(36) Owens, L; Cancer Res 1995, V55, P2752 HCAPLUS
(37) Ozawa, M; Mech Dev 1990, V33, P49 HCAPLUS
(38) Paine, T; Int J Cancer 1992, V50, P463 MEDLINE
(39) Pandey, A; J Biol Chem 1994, V269, P30154 HCAPLUS
(40) Pandey, A; J Biol Chem 1995, V270, P19201 HCAPLUS
(41) Pandey, A; Science (Washington DC) 1995, V268, P567 HCAPLUS
(42) Parsons, J; Curr Opin Cell Biol 1996, V8, P146 HCAPLUS
(43) Pasquale, E; Curr Opin Cell Biol 1997, V9, P608 HCAPLUS
(44) Pauley, R; Eur J Cancer Prev 1993, V2(Suppl 3), P67
(45) Press, M; Prog Clin Biol Res 1990, V354A, P209 MEDLINE
(46) Price, J; Breast Cancer Res Treat 1996, V39, P93 MEDLINE
(47) Roche, S; Curr Biol 1998, V8, P975 HCAPLUS
(48) Rosenberg, I; Am J Physiol 1997, V273, PG824 HCAPLUS
(49) Southern, P; J Mol Appl Genet 1982, V1, P327 HCAPLUS
(50) Stein, E; Genes Dev 1998, V12, P667 HCAPLUS
(51) Stein, E; J Biol Chem 1998, V273, P1303 HCAPLUS
(52) Takeichi, M; Curr Opin Cell Biol 1993, V5, P806 HCAPLUS
(53) van der Geer, P; Annu Rev Cell Biol 1994, V10, P251 HCAPLUS
(54) Vestweber, D; Cell Differ 1984, V15, P269 HCAPLUS
(55) Vestweber, D; EMBO J 1985, V4, P3393 HCAPLUS
(56) Vestweber, D; Exp Cell Res 1984, V152, P169 HCAPLUS
(57) Volberg, T; EMBO J 1992, V11, P1733 HCAPLUS
(58) Zhang, R; Invasion Metastasis 1991, V11, P204 MEDLINE
(59) Zisch, A; Cell Tissue Res 1997, V290, P217 HCAPLUS
(60) Zisch, A; Oncogene 1998, V16, P2657 HCAPLUS
    ANSWER 53 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
L40
AN
     1998:685118 HCAPLUS
DN
     129:310905
ED
     Entered STN: 29 Oct 1998
ΤI
     Study and treatment of diseases related to specific cellular functions of
     receptor protein tyrosine kinases
IN
     Clary, Douglas
PA
     Sugen, Inc., USA
     PCT Int. Appl., 81 pp.
so
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM G01N033-566
     ICS A61K031-00
CC
     1-12 (Pharmacology)
     Section cross-reference(s): 13, 14, 63
FAN.CNT 1
     PATENT NO.
                        KIND
                               DATE
                                           APPLICATION NO.
                                                                   DATE
                                           -----
                        ----
                                -----
ΡI
     WO 9845708
                         A1
                               19981015 WO 1998-US6842
                                                                  19980407 <--
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
            NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
            UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, ML, MR, NE, SN, TD, TG
     AU 9868876
                               19981030
                                         AU 1998-68876
                         A1
                                                                   19980407 <--
                                           US 1998-57150
     US 2002068361
                                20020606
                                                                   19980407 <--
                         A1
```

```
haddad - 10 / 823259
                                                                         Page 211
    US 6235769
                        B1
                              20010522
                                        US 1998-109883
                                                           19980702 <--
PRAI US 1997-43207P
                      P
                              19970408 <--
    US 1997-51715P
                              19970703 <--
                       P
    WO 1998-US6842
                       W
                              19980407 <--
CLASS
 PATENT NO.
             CLASS PATENT FAMILY CLASSIFICATION CODES
 ______
                      G01N033-566
WO 9845708
              ICM
               ICS A61K031-00
WO 9845708
              ECLA G01N033/566
                                                                         <--
US 2002068361 NCL 435/455.000; 435/007.100
                                                                         <--
US 6235769
              NCL
                       514/419.000; 514/418.000
                ECLA A61K031/40
    The invention relates to methods of evaluating the specific function of a
AB
    receptor protein tyrosine kinase in
    cells by activating the receptor in a ligand-independent
    fashion. In addition, the invention includes methods of identifying compds.
    that modulate receptor protein tyrosine
    kinase function. The invention also relates to a method of
    preventing or treating an abnormal condition caused by an
    aberration in the function of the C-RET receptor, and
    specifically to the treatment and prevention of
    neurodegenerative disorders by administering a compound that modulates the
    function of the C-RET receptor.
ST
    receptor protein tyrosine kinase
    function evaluation; drug screening receptor protein
    tyrosine kinase; ret receptor disease
    therapeutic; neurodegenerative disorder therapeutic ret receptor
    modulator
IT
    Chicken (Gallus domesticus)
       (RPTK extracellular region from; study and treatment of diseases
       related to specific cellular functions of receptor
       protein tyrosine kinases, and screening
       method)
IT
    Chimeric gene
    RL: BPR (Biological process); BSU (Biological study, unclassified); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
       (RPTK intra- and extracellular region-encoding; study and treatment of
       diseases related to specific cellular functions of receptor
       protein tyrosine kinases, and screening
       method)
IT
    Nervous system
       (amyotrophic lateral sclerosis; study and treatment of diseases related
       to specific cellular functions of receptor protein
       tyrosine kinases, and screening method)
IT
    Biological transport
       (blood-brain barrier; study and treatment of diseases related to
       specific cellular functions of receptor protein
       tyrosine kinases, and screening method)
IT
    Nervous system
       (degeneration; study and treatment of diseases related to specific
       cellular functions of receptor protein
       tyrosine kinases, and screening method)
ΙT
    Cytoprotective agents
       (neuroprotectants; study and treatment of diseases related to specific
       cellular functions of receptor protein
       tyrosine kinases, and screening method)
IT
    Anti-Alzheimer's agents
    Antiparkinsonian agents
    Apoptosis
```

```
Blood-brain barrier
    Drug delivery systems
    Drug screening
    Nervous system agents
    Phenotypes
        (study and treatment of diseases related to specific cellular functions
        of receptor protein tyrosine
       kinases, and screening method)
IT
        (sympathetic; study and treatment of diseases related to specific
        cellular functions of receptor protein
        tyrosine kinases, and screening method)
IT
    RL: BPR (Biological process); BSU (Biological study, unclassified); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (to RPTK extracellular region; study and treatment of diseases related
        to specific cellular functions of receptor protein
        tyrosine kinases, and screening method)
IT
    204003-90-7
                  204003-91-8
                                204003-96-3
                                             204003-97-4
                                                            204004-10-4
    204004-11-5
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (study and treatment of diseases related to specific cellular functions
       of receptor protein tyrosine
       kinases, and screening method)
IT
    79079-06-4, EGF receptor tyrosine kinase
    101463-26-7
                 127407-08-3, Receptor protein
    tyrosine kinase
                      141588-26-3, Ltk tyrosine
             142243-02-5, Erk receptor tyrosine
             144114-11-4, Ros receptor tyrosine
    kinase
            144247-17-6, Irr receptor tyrosine
    kinase
    kinase 146279-92-7, Ret receptor tyrosine
    kinase 146592-50-9, Hek kinase 147171-40-2, Tor
    receptor tyrosine kinase 148047-27-2, Sek
    kinase 149146-92-9, Trk kinase 149433-90-9, Elk
    receptor tyrosine kinase 149433-91-0
     , Eck kinase 149433-92-1, Eph
    receptor tyrosine kinase
                             150523-24-3, Cek9
    tyrosine kinase
                     153190-60-4, Tyro-10 kinase
    153190-63-7, Axl tyrosine kinase receptor
    154907-68-3, Tyro-3 kinase 156859-16-4, Ryk receptor
    tyrosine kinase 157857-23-3, Myk2 receptor
    tyrosine kinase 160995-45-9, Ehk1 receptor
    tyrosine kinase 162032-63-5, Ddr receptor
    tyrosine kinase 166433-56-3, Alk receptor
    tyrosine kinase 169277-51-4, Mer receptor
    tyrosine kinase 171715-11-0, Mdk1 receptor
    tyrosine kinase 177529-09-8, MCK-10 receptor
    tyrosine kinase 180615-67-2, Ehk2 receptor
                    185766-52-3, Cck-4 protein
    tyrosine kinase
    tyrosine kinase 204934-34-9, Hek2 receptor
    tyrosine kinase
                    214692-97-4, Ror2 receptor
    tyrosine kinase
                     214692-98-5, Ror1 receptor
    tyrosine kinase
                    216974-70-8, Myk1 receptor
    tyrosine kinase
                     248259-60-1, Eek receptor
    tyrosine kinase
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
    (Biological study); PROC (Process)
        (study and treatment of diseases related to specific cellular functions
```

of receptor protein tyrosine kinases, and screening method)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Braunger, J; ONCOGENE 1997, V14(22), P2619 HCAPLUS
- (2) McCloskey, P; CELL GROWTH AND DIFFERENTIATION 1994, V5(10) HCAPLUS
- (3) Obermeier, A; THE EMBO JOURNAL 1993, V12(3), P933 HCAPLUS
- (4) Pharmacia Spa; WO 9622976 A 1996 HCAPLUS
- (5) Sachs, M; THE JOURNAL OF CELL BIOLOGY 1996, V133(5), P1095 HCAPLUS
- (6) Santoro, M; MOLECULAR AND CELLULAR BIOLOGY 1994, V14(1), P663 HCAPLUS
- (7) Spaargaren, M; JOURNAL OF BIOLOGICAL CHEMISTRY 1991, V266(3), P1733 HCAPLUS
- (8) Trupp, M; NATURE 1996, V381, P785 HCAPLUS
- L40 ANSWER 54 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 1996:185898 HCAPLUS
- DN 124:252691
- ED Entered STN: 30 Mar 1996
- TI Germ-line inactivation of the murine Eck receptor tyrosine kinase by gene trap retroviral insertion
- AU Chen, Jin; Nachabah, Abudi; Scherer, Christina; Ganju, Pam; Reith, Alastair; Bronson, Rod; Ruley, H. Earl
- CS Dep. Microbiology, Immunology, Vanderbilt Univ. Sch. Med., Nashville, TN, 37232, USA
- SO Oncogene (1996), 12(5), 979-88 CODEN: ONCNES; ISSN: 0950-9232
- PB Stockton
- DT Journal
- LA English
- CC 3-6 (Biochemical Genetics)
 Section cross-reference(s): 13
- AB The present study characterized a mutation in the Eck receptor tyrosine kinase gene induced by the U3βgeo gene trap retrovirus. The mutation (ecki) was identified during an in vitro screen for proviruses that disrupt developmentally regulated genes in cultured ES cells. The germ-line ecki fusion gene was expressed in blastocyst and later restricted to the primitive streak, node and to regions of the hindbrain in 6.5-10.5 day embryos. This is identical to the pattern of Eck gene expression as determined by either in situ hybridization or immunostaining, suggesting that expression of the Eck promoter was not affected by provirus integration. The provirus inserted approx. 8 kb upstream of the 5' end of the published cDNA sequence, and 1.8 kb downstream of an alternatively spliced 5' exon. The ecki allele is essentially a null mutation since mutant mice are severely deficient for Eck protein as determined by Western blot anal. and in vitro kinase assays. Nevertheless, mice homozygous for the mutation did not exhibit any discernable phenotype. These results suggest that other members of the Eph family of receptor tyrosine kinases can functionally compensate for loss of Eck.
- ST gene eck receptor tyrosine kinase mutation; retrovirus gene trap receptor Eck mutation; sequence exon gene eck mouse
- IT Embryo

(germ-line inactivation of murine Eck receptor tyrosine kinase by gene trap retroviral insertion and its effects on development)

- IT Deoxyribonucleic acid sequences
 - (of gene eck exon 5.2 from mouse)
- IT Mouse

(Mus musculus, germ-line inactivation of murine Eck

```
receptor tyrosine kinase by gene trap
        retroviral insertion)
IT
     Gene, animal
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (eck, germ-line inactivation of murine Eck
        receptor tyrosine kinase by gene trap
        retroviral insertion)
     Animal growth regulator receptors
IT
       Receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (glycoprotein B61, gene eck, germ-line inactivation of murine
        Eck receptor tyrosine kinase by
        gene trap retroviral insertion)
IT
     Mutation
        (insertion, germ-line inactivation of murine Eck
        receptor tyrosine kinase by gene trap
        retroviral insertion)
IT
     Virus, animal
        (retro-, U3βgeo gene trap; germ-line inactivation of murine
        Eck receptor tyrosine kinase by
        gene trap retroviral insertion)
IT
     149433-91-0, Kinase (phosphorylating), gene eck
     protein
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); BIOL (Biological study);
     PROC (Process)
        (germ-line inactivation of murine Eck receptor
        tyrosine kinase by gene trap retroviral insertion)
     166931-97-1
IT
     RL: PRP (Properties)
        (nucleotide sequence; germ-line inactivation of murine Eck
        receptor tyrosine kinase by gene trap
        retroviral insertion)
L40 ANSWER 55 OF 55 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     1991:241599 HCAPLUS
DN
     114:241599
ED
     Entered STN: 28 Jun 1991
TI
     cDNA cloning and characterization of eck, an epithelial
     cell receptor protein-tyrosine
     kinase in the eph/elk family of protein
     kinases
AU
     Lindberg, Richard A.; Hunter, Tony
     Mol. Biol. Virol. Lab., Salk Inst. Biol. Stud., San Diego, CA, 92186-5800,
CS
SO
     Molecular and Cellular Biology (1990), 10(12), 6316-24
     CODEN: MCEBD4; ISSN: 0270-7306
DT
     Journal
LΑ
     English
CC
     3-3 (Biochemical Genetics)
     Section cross-reference(s): 7
     A human epithelial (HeLa) cDNA library was screened with degenerate
AB
     oligonucleotides designed to hybridize to highly conserved regions of
     protein-tyrosine kinases. One cDNA from this
     screen was shown to contain a putative protein-tyrosine
     kinase catalytic domain and subsequently used to isolate another
     cDNA from a human keratinocyte library that encompasses the entire coding
     region of a 976-amino-acid polypeptide. The predicted protein
```

```
has an external domain of 534 amino acids with a presumptive N-terminal
     signal peptide, a transmembrane domain, and a cytoplasmic domain of 418
     amino acids that includes a canonical protein-tyrosine
     kinase catalytic domain. Mol. phylogeny indicates that this
     protein kinase is closely related to eph and
     elk and that this receptor family is more closely related to the
     non-receptor protein-tyrosine kinase
     families than to other receptor protein-
     tyrosine kinases. Antibodies raised against a TrpE
     fusion protein immunopptd. a 130-kDa protein that
     became phosphorylated on tyrosine in immune complex
     kinase assays, indicating that this protein is a bona
     fide protein-tyrosine kinase. Anal. of RNA
     from 13 adult rat organs showed that the eck gene is expressed
     most highly in tissues that contain a high proportion of epithelial cells,
     e.g., skin, intestine, lung, and ovary. Several cell lines of epithelial
     origin were found to express the eck protein
     kinase at the protein and RNA levels. Immunohistochem.
     anal. of several rat organs also showed staining in epithelial cells.
     These observations lead to the naming of this protein
     kinase eck, for epithelial cell kinase.
     epithelial all protein kinase eck sequence;
     cDNA eck protein kinase cloning sequence;
     human eck protein kinase cDNA sequence
IT
     HeLa cell
        (epithelial cell gene eck protein tyrosine
        kinase of, cloning and sequencing of cDNA for)
IT
     Epithelium
        (gene eck protein tyrosine kinase
        of, of human, cloning and sequencing of cDNA for)
IT
        (gene eck protein tyrosine kinase
        of, characterization of)
IT
     Intestine, composition
     Lung, composition
     Ovary, composition
        (gene eck protein tyrosine kinase
        of, of human, identification of)
IT
     Molecular cloning
        (of gene eck protein tyrosine
        kinase gene, of human epithelial cells)
     Protein sequences
IT
        (of gene eck protein tyrosine
        kinase and precursor, of human, complete)
IT
     Phosphorylation, biological
        (auto-, of gene eck protein tyrosine
        kinase, of human)
IT
     Skin, composition
        (epithelium, gene eck protein tyrosine
        kinase, of human, identification of)
IT
    Deoxyribonucleic acid sequences
        (protein (tyrosine) kinase-specifying,
        gene eck, of human, complete)
IT
     Gene and Genetic element, animal
     RL: BIOL (Biological study)
        (eck, for protein tyrosine kinase
        of human epithelial cells, cloning and sequencing of)
IT
     134090-19-0
                  134090-20-3
     RL: PRP (Properties)
        (amino acid sequence of)
```

```
IT
     80449-02-1
     RL: PRP (Properties)
        (gene eck, cDNA for, of human epithelial cell, cloning and
        sequence of)
IT
     134094-00-1
     RL: PRP (Properties); BIOL (Biological study)
        (nucleotide sequence of)
IT
     134093-99-5, Deoxyribonucleic acid (human clone OB18 gene eck
     protein (tyrosine) kinase messenger
     RNA-complementary)
     RL: PRP (Properties)
        (nucleotide sequences)
=> => d 126 bib abs retable tot
    ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
L26
AN
     2005:547699 HCAPLUS
TI
     Targeted drug delivery using epha2 or eph4 binding moieties
IN
    Kinch, Michael S.
PA
    Medimmune, Inc., USA
SO
    PCT Int. Appl., 231 pp.
    CODEN: PIXXD2
DT
    Patent
    English
LA
FAN.CNT 2
     PATENT NO.
                        KIND
                                           APPLICATION NO.
                               DATE
                                                                  DATE
                               -----
                        ----
                                           -----
                                                                  -----
PΙ
    WO 2005056766
                        A2
                              20050623 WO 2004-US41020
                                                                  20041206
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
            RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
            MR, NE, SN, TD, TG
PRAI US 2003-527396P
                         Р
                               20031204
    US 2004-4794
                         Α
                               20041203
    US 2004-4795
                               20041203
                         Α
    The present invention relates to methods and compositions designed for the
AB
    treatment, management, or prevention of a hyperproliferative cell disease,
    particularly cancer. The methods of the invention comprise the
    administration of an effective amount of a composition that targets cells
    expressing an Eph family receptor tyrosine kinase, such as EphA2
    or EphA4, for the treatment, management, or prevention of
    hyperproliferative diseases, particularly cancer. In one embodiment, the
    method of the invention comprises administering to a subject a composition
    comprising an EphA2 or EphA4 targeting moiety attached to a
    delivery vehicle, and one or more therapeutic or prophylactic agents that
    treat or prevent a hyperproliferative disease, where the therapeutic or
    prophylactic agents that treat or prevent a hyperproliferative disease,
    where the therapeutic or prophylactic agents are operatively associated
```

with the delivery vehicle. In another embodiment, the method of the invention comprises administering to a subject a composition comprising a

or EohA4 targeting moiety and a therapeutic or prophylactic agent that

nucleic acid comprising a nucleotide sequence encoding an EphA2

treats or prevents a hyperproliferative disease. In yet another embodiment, the method of the invention comprises administering to a subject a composition comprising an EphA2 or EphA4 targeting moiety and a nucleic acid comprising a nucleotide sequence encoding an agent that treats or prevents a hyperproliferative disease, where the nucleic acid is operatively associated with the delivery vehicle. Pharmaceutical compositions are also provided by the present invention.

ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN

L26

2005:540463 HCAPLUS

AN

```
TI
     EphA2-, ephA4-, and low molecular weight protein tyrosine
    phosphatase-based methods for treatment of hyperproliferative cell
    disorders
IN
    Kinch, Michael S.
PA
    Medimmune, Inc., USA
SO
    PCT Int. Appl., 240 pp.
    CODEN: PIXXD2
DT
    Patent
    English
LA
FAN.CNT 2
    PATENT NO.
                        KIND
                               DATE
                                           APPLICATION NO.
                                                                  DATE
                                           -----
PΙ
    WO 2005055948
                        A2
                               20050623 WO 2004-US41023
                                                                 20041206
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
            MR, NE, SN, TD, TG
PRAI US 2003-527154P
                         P
                               20031204
    US 2004-4794
                         Α
                               20041203
    US 2004-4795
                               20041203
                         Α
AB
    The invention discloses methods and compns. designed for treatment,
    management, or prevention of a hyperproliferative cell disease, in
```

particular cancer. The methods comprise the administration of an effective amount of a composition that targets cells expressing low mol. weight protein tyrosine phosphatase (LMW-PTP) in particular using moieties that bind an Eph family receptor tyrosine kinase, such as EphA2 or EphA4, and inhibits or reduces LMW-PTP expression and/or activity. embodiment, the method comprises administering to a subject a composition comprising an EphA2 or EphA4 targeting moiety attached to a delivery vehicle, and one or more agents that inhibit LMW-PTP expression and/or activity operatively associated with the delivery vehicle. In another embodiment, the method comprises administering to a subject a composition comprising a nucleic acid comprising a nucleotide sequence encoding an EphA2 or EphA4 targeting moiety and an agent that inhibits or reduces LMW-PTP expression and/or activity. In yet another embodiment, the method comprises administering to a subject a composition comprising an EphA2 or EphA4 targeting moiety and a nucleic acid comprising a nucleotide sequence encoding an agent that inhibits or reduces LMW-PTP expression and/or activity, where the nucleic acid is operatively associated with the delivery vehicle. Pharmaceutical compns. are also provided by the invention.

L26 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN

```
2005:493472 HCAPLUS
AN
TI
     EphA2 agonistic monoclonal antibodies for diagnosis, prognosis
     and therapy of cancer and metastasis
IN
     Kinch, Michael S.; Carles-Kinch, Kelly; Stewart, Jane C.
PA
     Medimmune, Inc., USA; Purdue Research Foundation
     PCT Int. Appl., 134 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                        KIND
                               DATE
                                          APPLICATION NO.
                                                                 DATE
                        ----
                                         -----
     -----
                              -----
                                                               -----
                       A2 20050609 WO 2004-US39112 20041119
    WO 2005051307
ΡI
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
            SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
            NE, SN, TD, TG
PRAI US 2003-524177P
                        P
                               20031120
     The present invention relates to methods and compns. designed for the
     treatment, management, or prevention of cancer, particularly, metastatic
     cancer. The methods of the invention comprise the administration of an
     effective amount of one or more antibodies that bind to and agonize
     EphA2, thereby increasing EphA2 phosphorylation and
     decreasing EphA2 levels in cells which EphA2 has been
     agonized. The invention also encompasses antibodies that preferentially
     bind an EphA2 epitope exposed on cancer cells but not non-cancer
     cells. The invention also provides pharmaceutical compns. comprising one
     or more EphA2 antibodies of the invention either alone or in
     combination with one or more other agents useful for cancer therapy. In
     addition, diagnostic methods and methods for screening for therapeutically
     useful anti-EphA2 antibodies are also provided.
L26
    ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
     2005:371065 HCAPLUS
AN
DN
     142:409704
ΤI
     Recombinant Listeria encoding EphA2 antigen peptides as vaccines
     against cancer and proliferative diseases
IN
    Kinch, Michael S.; Kiener, Peter A.; Bruckheimer,
    Elisabeth; Dubensky, Thomas W., Jr.; Cook, David N.
PA
    Medimmune, Inc., USA; Cerus Corporation
SO
     PCT Int. Appl., 219 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 4
     PATENT NO.
                        KIND
                               DATE
                                         APPLICATION NO.
                             -----
                                                                 -----
     -----
                        ----
                                         -----
                        A2 20050428 WO 2004-US34694
PΙ
    WO 2005037233
                                                               20041015
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
```

```
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
PRAI US 2003-511719P
                          Р
                                20031015
     US 2003-511919P
                          Ρ
                                20031015
     US 2003-532666P
                          ₽
                                20031224
     US 2004-556631P
                         P
                                20040326
     US 2004-615470P
                         P
                                20041001
     US 2004-617544P
                         Ρ
                                20041007
AB
```

The present invention relates to methods and compns. designed for the treatment, management, or prevention of cancer, particularly metastatic cancer and cancers of T cell origin, and hyperproliferative diseases involving EphA2-expressing cells. The methods of the invention entail the use of a Listeria-based EphA2 vaccine. The invention also provides pharmaceutical compns. comprising one or more Listeria-based vaccines of the invention either alone in combination with one or more other agents useful for cancer therapy. In certain aspects of the invention, the method entail eliciting both CD4+ and CD8+ T-cell responses against EphA2 and/or EphA2-expressing cells.

```
L26
    ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
```

AN 2005:343316 HCAPLUS

ΤI Antibody humanization by framework shuffling

ΑU Dall'Acqua, William F.; Damschroder, Melissa M.; Zhang, Jingli; Woods, Robert M.; Widjaja, Lusiana; Yu, Julie; Wu, Herren

CS Department of Antibody Discovery and Protein Engineering, MedImmune, Inc., Gaithersburg, MD, 20878, USA

SO Methods (San Diego, CA, United States) (2005), 36(1), 43-60 CODEN: MTHDE9; ISSN: 1046-2023

PB Elsevier

DT Journal

LA English

AB We report here the humanization of a mouse monoclonal antibody (mAb B233) using a new technique which we call framework shuffling. MAb B233 was raised against the human receptor tyrosine kinase EphA2 which is selectively up-regulated in many cancer cell lines and as such constitutes an attractive target for cancer therapy. The six CDRs of B233 were fused in-frame to pools of corresponding individual human frameworks. human frameworks encompassed all known heavy and light (κ) chain human germline genes. The resulting Fab combinatorial libraries were then screened for binding to the antigen. A two-step selection process, in which the light and heavy chains of the parental mAb were successively humanized, resulted in the identification of several humanized variants that retained binding to EphA2. More precisely, after conversion to human IgG1, the dissociation consts. of three select fully humanized variants ranged from 3 to 48 nM. This brings the best framework-shuffled, humanized binder within 5-fold of the avidity of parental mAb B233. Importantly, these humanized IgGs also possessed biochem. activities similar to those of parental mAb B233 as judged by induction of EphA2 phosphorylation. Thus, without requiring any rational design or structural information, this new humanization approach allows to rapidly identify various human framework combinations able to support the structural feature(s) of the CDRs which are essential for binding and functional activity.

RETABLE

```
Referenced Author
                    |Year | VOL | PG
                                       | Referenced Work
                                                             Referenced
                    (RPY) (RVL) (RPG)
      (RAU)
                                              (RWK)
                                                             File
```

```
__________________
Amit, A
                       1986 233
                                   747
                                          Science
                                                               HCAPLUS
                                          Proteins
Banfield, M
                       1997
                             129
                                   161
                                                               HCAPLUS
                                          Proc Natl Acad Sci U HCAPLUS
Benhar, I
                       1994
                             91
                                   12051
Boshart, M
                       1985
                                   521
                                           Cell
                                                               HCAPLUS
                             41
Boulianne, G
                       1984
                             312
                                   643
                                          Nature
                                                               HCAPLUS
Brensing-Kuppers, J
                       1997
                             191
                                   173
                                           Gene
                                                               HCAPLUS
Carles-Krunvainch, K
                       2002
                             62
                                   2840
                                           Cancer Res
                       1992
                             89
                                    4285
                                          Proc Natl Acad Sci U | HCAPLUS
Carter, P
                       2003
                                    7907
Coffman, K
                             63
                                           Cancer Res
                                                               HCAPLUS
                       1972
                                           Immunochemistry
                                                               HCAPLUS
Crothers, D
                                    341
Eigenbrot, C
                       1994
                             18
                                    49
                                          Proteins
                                                               HCAPLUS
                                    487
                                           J Mol Biol
                                                               HCAPLUS
Foote, J
                       1992
                             224
                                    99
                                          Antibody Therapeutic
Harris, W
                       1995
                             17
                                    3055
                                          Anticancer Res
                                                               MEDLINE
Hasholzner, U
                       1997
Hieter, P
                       1982
                             257
                                    1516
                                           J Biol Chem
                                                               HCAPLUS
                       1989
                                          Gene
                                                               HCAPLUS
Ho, S
                             77
                                    51
Holmes, M
                       1997
                             158
                                    2192
                                           J Immunol
                                                               HCAPLUS
                                           J Infect Dis
Johnson, S
                       1997
                             176
                                    1215
                                                               HCAPLUS
                                          Anal Biochem
Johnsson, B
                       1991
                             198
                                    268
                                                               HCAPLUS
                                                               HCAPLUS
                       1986
                             321
                                    522
                                          Nature
Jones, P
                                          Sequences of Protein
                       1991
Kabat, E
                       1991
                                    773
                                          Protein Eng
                                                               HCAPLUS
Kettleborough, C
                                          Arch Pathol Lab Med
                                                               HCAPLUS
Klee, G
                       2000
                             124
                                    921
                                                               MEDLINE
                       1975
                             256
                                    495
                                          Nature
Kohler, G
                                          Methods Enzymol
                                                                HCAPLUS
Kunkel, T
                       1987
                             154
                                    367
                                           Clin Diagn Lab Immun | MEDLINE
                       1994
                                    365
Kuus-Reichel, K
                             1
                       1998
                             188
                                    1973
                                           J Exp Med
Matsuda, F
Muller, K
                       1998
                             261
                                    149
                                           Anal Biochem
                                                               HCAPLUS
                                           Mol Immunol
Padlan, E
                        1991
                             28
                                    489
                                                               HCAPLUS
Pichla, S
                        1997
                             119
                                    6
                                           J Struct Biol
                                                               HCAPLUS
Presta, L
                        1993
                             151
                                   2623
                                           J Immunol
                                                                HCAPLUS
                        1989
                                          |Proc Natl Acad Sci U|HCAPLUS
                                    10029
Queen, C
                             186
                             27
                                    583
                                           Cell
                                                                MEDLINE
                        1981
Ravetch, J
                                           J Biol Chem
                        1996
                             271
                                    22611
                                                                HCAPLUS
Rosok, M
                                          Eur J Immunol
                                                                HCAPLUS
                                    2717
Routledge, E
                        1991
                             121
                                           Proc Natl Acad Sci U HCAPLUS
                       1977
                             74
                                    5463
Sanger, F
                                           Biol Chem Hoppe Seyl MEDLINE
                       1993
                             374
                                    1001
Schable, K
                       1991
                             147
                                    4366
                                           J Immunol
                                                                MEDLINE
Shearman, C
                       2002
                                           J Immunol
                                                                HCAPLUS
                             169
                                    1119
Tan, P
Tangri, S
                       2002
                                    2191
                                           Curr Med Chem
                                                               HCAPLUS
                                           J Mol Biol
                                                               HCAPLUS
                        1990
                             215
                                    175
Tramontano, A
                                                                HCAPLUS
                        1988
                             1239
                                    1534
                                           Science
Verhoeyen, M
                                           Methods Mol Biol
                                                               HCAPLUS
                             207
                                    197
Wu, H
                        2003
                                   213
                                          |Methods Mol Biol
                                                               | HCAPLUS
                       2003
                             1207
Wu, H
     ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
L26
     2005:182287 HCAPLUS
AN
     142:278743
DN
     Humanization of antibodies by combinatorial library technology for
ΤI
     immunodiagnosis and immunotherapy or gene therapy
     Wu, Herren; Dall-Acqua, William; Damschroder, Melissa
IN
     Medimmune, Inc., USA
PA
     U.S. Pat. Appl. Publ., 130 pp.
SO
     CODEN: USXXCO
DT
     Patent
LA
     English
FAN.CNT 1
                                                                   DATE
                                            APPLICATION NO.
     PATENT NO.
                         KIND
                                DATE
     _____
                         ----
```

```
PΙ
     US 2005048617
                           A1
                                  20050303
                                               US 2004-920899
                                                                        20040818
     WO 2005042743
                                  20050512
                                               WO 2004-US26953
                           A2
                                                                       20040818
              AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
              CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
              GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
              LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
              NO; NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
              TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
              AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
              EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
              SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
              SN, TD, TG
PRAI US 2003-496367P
                           Ρ
                                  20030818
     The present invention relates to methods of reengineering or reshaping
     antibodies to reduce the immunogenicity of the antibodies, while
     maintaining the immunospecificity of the antibodies for an antigen.
     particular, the present invention provides methods of producing antibodies
     immunospecific for an antigen by synthesizing a combinatorial library
     comprising complementarity determining regions (CDRs) from a donor antibody
     fused in frame to framework regions from a sub-bank of framework regions.
     The present invention also provides antibodies produced by the methods of
     the invention. Thus, preparation of humanize anti-human EphA2
     monoclonal antibodies B233 was exemplified.
L26
     ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2005:161005 HCAPLUS
DN
     142:254576
ΤI
     Inhibitors of EphA2, PCDGF, and HAAH for combination therapy and
     diagnosis of prevention of hyperproliferative disorder, cancer and
     metastasis
IN
     Kinch, Michael S.; Carles-Kinch, Kelly; Kiener, Peter;
     Langermann, Solomon; Mccarthy, Michael P.; Tice, David; Woessner,
     Richard
PA
     Medimmune, Inc., USA
so
     PCT Int. Appl., 177 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                          KIND
                                  DATE
                                               APPLICATION NO.
                                                                       DATE
                          ----
                                  _____
                                              -----
                                                                       -----
PΤ
     WO 2005016381
                           A2
                                             WO 2004-US23097
                                  20050224
                                                                       20040716
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
         TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
              SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
              SN, TD, TG
PRAI US 2003-489036P
                          , P
                                  20030721
     The present invention relates to methods and compns. designed for the
     treatment, management, or prevention of a hyperproliferative disorder,
     particularly cancer, more particularly metastatic cancer. The methods of
     the invention comprise the administration of an effective amount of one or
     more agents that decrease/inhibit EphA2 receptor tyrosine kinase
```

(EphA2) expression or activity in combination with one or more agents that decrease/inhibit PC cell derived growth factor (PCDGF) or human aspartyl (asparaginyl) β -hydroxylase (HAAH) expression or activity. In another embodiment, the methods of the invention comprise the administration of an effective amount of one or more EphA2, PCDGF, and/or HAAH agents of the invention that inhibit cancer cell colony formation in soft agar or tubular network formation in three-dimensional basement membrane or extracellular matrix preparation. The invention also provides pharmaceutical compns. comprising one or more EphA2 agents of the invention in combination with one or more PCDGF agents of the invention and/or one or more HAAH agents of the invention. In some embodiments, the agents of the invention can be administered with other cancer therapeutic agents that are not EphA2-, PCDGF-, or HAAH-based. Diagnostic methods and methods for screening for therapeutically useful agents of the invention are also provided.

```
ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
L26
AN
    2005:160740 HCAPLUS
DN
    142:259976
    Combinatorial preparation of humanized anti-interleukin 9 and anti-human
TI
    EphA2 monoclonal antibodies, fragments and conjugates for
    screening, diagnosis and therapy
    Wu, Herren; Dall-Acqua, William; Damschroder, Melissa
IN
PA
    Medimmune, Inc., USA
SO
    U.S. Pat. Appl. Publ., 179 pp.
    CODEN: USXXCO
DT
    Patent
LA
    English
FAN.CNT 1
    PATENT NO.
                       KIND
                             DATE
                                         APPLICATION NO.
                                                                DATE
                        ----
                               -----
                                          -----
PΙ
    US 2005042664
                        A1
                               20050224
                                          US 2004-923068
                                                                20040820
    WO 2005035575
                        A2
                              20050421
                                         WO 2004-US27188
                                                                20040820
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
```

SN, TD, TG
PRAI US 2003-497213P P 20030822
US 2003-510741P P 20031013

AB The present invention provides methods of re-engineering or re-shaping an antibody from a first species, wherein the re-engineered or re-shaped antibody does not elicit undesired immune response in a second species, and the re-engineered or re-shaped antibody retains substantially the same antigen binding-ability of the antibody from the first species. In accordance with the present invention, a combinatorial library comprising the CDRs of the antibody from the first species fused in frame with framework regions derived from a second species can be constructed and screened for the desired modified antibody heavy and light chains. In particular, the present invention provides methods utilizing low homol. acceptor antibody frameworks for efficiently humanizing an antibody or a fragment thereof. The present invention also provides antibodies produced by the methods of the invention.

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

```
L26
     ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2005:120967 HCAPLUS
DN
     142:217364
ΤI
     Human EphA2 protein T cell epitope agonists for ELISPOT assay
     and as vaccines against tumor overexpressing EphA2
IN
     Storkus, Walter J.; Kinch, Michael S.
PA
     University of Pittsburgh-of the Commonwealth System of Higher Education,
     USA; Medimmune, Inc.
SO
     PCT Int. Appl., 115 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                        KIND
                                DATE
                                           APPLICATION NO.
                                                                   DATE
     -----
                         ----
                                -----
                                            -----
PΙ
     WO 2005012350
                         A2
                                20050210
                                           WO 2004-US23931
                                                                   20040722
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     US 2005048550
                         A1
                                20050303
                                            US 2004-897711
                                                                   20040722
PRAI US 2003-491046P
                         P
                                20030730
     EphA2 T-cell epitope agonists are provided herein. The agonists
     include peptides corresponding to specific fragments of human
     EphA2 protein containing one or more T-cell epitopes, and conservative
     derivs. thereof. The EphA2 T-cell epitope agonists are useful
     in an assay, such as an ELISPOT assay, that may be used to determine and/or
     quantify a patient's immune responsiveness to EphA2. The
     agonists also are useful in methods of modulating a patient's immune
     reactivity to EphA2, which has substantial utility as a
     treatment for cancers that overexpress EphA2, such as renal cell
     carcinoma. The EphA2 agonists also can be used to vaccinate a
     patient against EphA2, by in vivo or ex vivo methods.
L26
    ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2005:103328 HCAPLUS
ΤI
     Expression of EphA2 is prognostic of disease-free interval and
     overall survival in surgically treated patients with renal cell carcinoma
     Herrem, Christopher J.; Tatsumi, Tomohide; Olson, Kathleen S.; Shirai,
     Keisuke; Finke, James H.; Bukowski, Ronald M.; Zhou, Ming; Richmond, Amy
     L.; Derweesh, Ithaar; Kinch, Michael S.; Storkus, Walter J.
CS
     Department of Immunology, University of Pittsburgh School of Medicine,
     Pittsburgh, PA, USA
SO
     Clinical Cancer Research (2005), 11(1), 226-231
     CODEN: CCREF4; ISSN: 1078-0432
     American Association for Cancer Research
PB
DΤ
     Journal
LΑ
     English
     Whereas normally expressed at sites of cell-to-cell contact in adult
AB
     epithelial tissues, recent studies have shown that the receptor tyrosine
     kinase EphA2 is overexpressed in numerous epithelial-type
     carcinomas, with the greatest level of EphA2 expression observed in
     metastatic lesions. In the current study, we have assessed EphA2
```

expression in archived renal cell carcinoma (RCC) tissues as it relates to patient disease course. Using specific anti-EphA2 monoclonal antibody 208 and immunohistochem. we evaluated EphA2 protein expression levels in RCC specimens surgically resected from 34 patients (including 30 conventional clear-cell RCC, 3 papillary, and 1 chromophobic RCC cases) resulting in clin. cures. Regardless of histopathol. subtype, RCC lesions expressing higher levels of EphA2 tended to be of a higher grade (P < 0.05) and larger (P = 0.093), more-highly-vascularized tumors (P = 0.005). Perhaps most notable, the degree of EphA2 overexpression (vs. normal matched autologous kidney tissue) seemed predictive of short-term (<1 yr) vs. longer-term (≥1 yr) disease-free interval (P < 0.001) and of overall survival (P < 0.001) among the RCC patients evaluated. These data suggest that EphA2 expression level may serve as a useful prognostic tool in the clin. management of patients who have been successfully treated with surgery, but who are at greater risk for accelerated disease recurrence and who have a poorer prognosis.

n	E٦	תיח	D	т	1
•	г.		חו		

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Brantley, D	2002	21	7011	Oncogéne	HCAPLUS
DeRisi, J	1996	14	457	Nat Genet	HCAPLUS
Duxbury, M	2004	23	1448	Oncogene	HCAPLUS
D'Amico, T	2001	72	1144	Ann Thorac Surg	MEDLINE
Easty, D	1995	55	2528	Cancer Res	HCAPLUS
Easty, D	1999	84	494	Int J Cancer	HCAPLUS
Eble, J	2004	İ	ĺ	WHO classification o	İ
Hendrix, M	2003	22	3070	Oncogene	HCAPLUS
Kataoka, H	2004	95	136	Cancer Sci	HCAPLUS
Kikawa, K	2002	277	39274	J Biol Chem	HCAPLUS
Kinch, M	2003	9	613	Clin Cancer Res	HCAPLUS
Kinch, M	2003	20	59	Clin Exp Metastasis	HCAPLUS
Lu, M	2003	63	3425	Cancer Res	HCAPLUS
Mellitzer, G	2000	10	400	Curr Opin Neurobiol	HCAPLUS
Miyazaki, T	2003	103	657	Int J Cancer	HCAPLUS
Ogawa, K	2000	19	6043	Oncogene	HCAPLUS
Stein, E	1998	12	667	Genes Dev	HCAPLUS
Straume, O	2002	160	1009	Am J Pathol	HCAPLUS
Tatsumi, T	2003	63	4481	Cancer Res	HCAPLUS
Thaker, P	2004	10	5145	Clin Cancer Res	HCAPLUS
Walker-Daniels, J	2003	162	1037	Am J Pathol	HCAPLUS
Walker-Daniels, J	1999	41	275	Prostate	HCAPLUS
Zantek, N	1999	10	629	Cell Growth Differ	HCAPLUS
Zelinski, D	2001	61	2301	Cancer Res	HCAPLUS
Zelinski, D	2002	85	714	J Cell Biochem	HCAPLUS
Zeng, G	2003	163	2271	Am J Pathol	HCAPLUS

```
L26 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
```

AN 2005:59831 HCAPLUS

DN 142:154248

TI Anti-EphA4 antibodies and agonists for diagnosis, prognosis and treatment of cancer and metastasis

IN Kinch, Michael S.; Carles-Kinch, Kelly

PA USA

SO U.S. Pat. Appl. Publ., 59 pp. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

```
PATENT NO.
                       KIND
                              DATE
                                        APPLICATION NO.
                                                               DATE
     -----
                       ____
                              -----
                                         -----
                                                               _____
                              20050120 US 2004-863729
                       A1
PΙ
    US 2005013819
                                                                20040607
    WO 2005048917
                       A2
                              20050602 WO 2004-US18279
           AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
            SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
            SN, TD, TG
PRAI US 2003-476909P
                        Ρ
                              20030606
    US 2003-503356P
                        P
                              20030916
```

AB The present invention relates to methods and compns. designed for the treatment, management, or prevention of cancer, particularly, metastatic cancer. In one embodiment, the methods of the invention comprise the administration of an effective amount of one or more antibodies that bind to EphA4 and agonize EphA4. In another embodiment, the methods of the invention comprise the administration of an effective amount of one or more antibodies that bind to EphA4 and inhibit cancer cell colony formation in soft agar or tubular network formation in three-dimensional basement membrane or extracellular matrix preparation. In another embodiment, the methods of the invention comprise the administration of an effective amount of one or more antibodies that preferentially binds to an EphA4 epitope that is exposed on cancer cells but not non-cancer cells. In another embodiment, the methods of the invention comprise the administration of an effective amount of one or more antibodies that bind to EphA4 with a very low Koff to reduce EphA4 expression and, thereby, inhibit tumor cell growth and/or metastasis. The invention also provides pharmaceutical

compns. comprising one or more EphA4 antibodies of the invention either alone or in combination with one or more other agents useful for cancer

- L26 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2004:930662 HCAPLUS
- DN 142:86069

therapy.

- TI Decreased tumorigenic potential of **EphA2**-overexpressing breast cancer cells following treatment with adenoviral vectors that express EphrinA1
- AU Noblitt, Loren W.; Bangari, Dinesh S.; Shukla, Shruti; Knapp, Deborah W.; Mohammed, Sulma; Kinch, Michael S.; Mittal, Suresh K.
- CS Laboratory of Gene Therapy, Purdue University, West Lafayette, IN, 47907, USA
- SO Cancer Gene Therapy (2004), 11(11), 757-766 CODEN: CGTHEG; ISSN: 0929-1903
- PB Nature Publishing Group
- DT Journal
- LA English
- AB The EphA2 receptor tyrosine kinase is frequently overexpressed in invasive breast cancer cells. Moreover, these malignant cells have unstable cell-cell contacts, which preclude EphA2 from interacting with its ligand, EphrinA1, which is anchored to the membrane of adjacent cells. This defect is important because ligand binding causes EphA2 to transmit signals that neg. regulate tumor cell growth and survival, whereas the absence of ligand binding favors these same behaviors. In our present study, human adenoviral type 5 (HAd) vectors

were engineered to express secreted-forms of EphrinA1. These vectors were used to infect MDA-MB-231 human breast cancer cells, or MCF-10A human breast epithelial cells providing matched controls. Infection with HAd-EphrinA1-Fc (HAd vector expressing extracellular domain of human EphrinA1 attached to Fc portion of human IgG1 heavy chain) caused increased EphA2 activation and turnover and consequently decreased tumor cell viability in soft agar assays. Consistent with this observation, infection of MDA-MB-231 cells with HAd-EphrinA1-Fc prevented tumor formation in xenograft models. Furthermore, therapeutic modeling via intratumoral inoculation revealed that HAd-EphrinA1-Fc significantly inhibited subsequent tumor growth as compared to matched controls. These results suggest that targeting of EphA2 with adenoviral vectors may have therapeutic value.

RETABLE	
---------	--

RETABLE					
Referenced Author		NOT		Referenced Work	Referenced
(RAU)	(RPY)	(RVL)	(RPG)	(RWK)	File
	+=====	+=====	+=====	+======================================	
Addison, C	1995	92	8522	Proc Natl Acad Sci U	HCAPLUS
Akbulut, H	2003	10	388	Cancer Gene Ther	HCAPLUS
Ambar, B	1999	10	1641	Hum Gene Ther	HCAPLUS
Andres, A	1995	63	288	Int J Cancer	HCAPLUS
Bangari, D	2004			Virus Res, in press	
Bartley, T	1994	368	558	Nature	HCAPLUS
Carles-Kinch, K	2002	62	2840	Cancer Res	HCAPLUS
Chen, L	1996	22	477	Somat Cell Mol Genet	HCAPLUS
Coffman, K	2003	63	7907	Cancer Res	HCAPLUS
Curiel, D	2000	6	3395	Clin Cancer Res	HCAPLUS
Dickson, R	1995	16	559	Endocr Rev	HCAPLUS
Ding, Y	2002	8	3290	Clin Cancer Res	HCAPLUS
Dohn, M	2001	20	6503	Oncogene	HCAPLUS
Easty, D	1995	55	2528	Cancer Res	HCAPLUS
George, J	2003	10	1135	Gene Therapy	
Graham, F	1977	36	59	J Gen Virol	MEDLINE
Graham, F	1991		109	Methods of Molecular	HCAPLUS
Graham, F	1973	52	456	Virology	MEDLINE
Hitt, M	2000	55	479	Adv Virus Res	HCAPLUS
Kikawa, K	2002	277	39274	J Biol Chem	HCAPLUS
Kinch, M	2003	20	59	Clin Exp Metast	HCAPLUS
Kinch, M	1998	17	227	Hybridoma	HCAPLUS
Koolpe, M	2002	277	46974	J Biol Chem	HCAPLUS
Kullander, K	2001	29	73	Neuron	HCAPLUS
Liu, Y	2002	9	202	Cancer Gene Ther	HCAPLUS
Liu, Y	2002	9	533	Cancer Gene Ther	HCAPLUS
Miao, H	2001	3	527	Nat Cell Biol	HCAPLUS
Ng, P	1999	10	2667	Hum Gene Ther	HCAPLUS
Palmer, K	2001	8	282	Gene Therapy	HCAPLUS
Parks, R	1999	6	1565	Gene Therapy	HCAPLUS
Price, J	1986	77	529	J Natl Cancer Inst	MEDLINE
Rosenberg, I	1997	273	G824	Am J Physiol	HCAPLUS
Sambrook, J	2001			Molecular Cloning:A	
Stewart, A	1999	6	350	Gene Therapy	HCAPLUS
Trudel, S	2001	15	846	Leukemia	HCAPLUS
Vlachaki, M	2001	51	1008	Int J Radiat Oncol B	HCAPLUS
Walker-Daniels, J	2003	162	1037	Am J Pathol	HCAPLUS
Walker-Daniels, J	1999	41	275	Prostate	HCAPLUS
Wen, X	2001	8	361	Cancer Gene Ther	HCAPLUS
Zantek, N	1999	10	629	Cell Growth Differ	HCAPLUS
Zelinski, D	2001	61	2301	Cancer Res	HCAPLUS
Zisch, A	2000	19	177	Oncogene	HCAPLUS

- L26 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2004:878784 HCAPLUS
- DN 142:4180
- TI EphA2 Induction of Fibronectin Creates a Permissive Microenvironment for Malignant Cells
- AU Hu, Min; Carles-Kinch, Kelly L.; Zelinski, Daniel P.; Kinch, Michael S.
- CS Department of Basic Medical Sciences, Purdue University Cancer Center, Gaithersburg, MD, USA
- SO Molecular Cancer Research (2004), 2(10), 533-540 CODEN: MCROC5; ISSN: 1541-7786
- PB American Association for Cancer Research
- DT Journal
- LA English
- Normal and metastatic cells continuously exchange information with the AB surrounding tissue environment, and this communication governs many aspects of cell behavior. In particular, the phys. placement or adhesions of cells within their environment are increasingly understood to facilitate this communication. Classically, cell-cell and cell-extracellular matrix adhesions have been viewed as separable events that are independently controlled. This simple view is changing, as evidence emerges of coordinated regulation of cellular adhesions. Here, the authors show that the EphA2 tyrosine kinase, which is overexpressed in many aggressive cancers, regulates a fine balance of cell-cell and cell-extracellular matrix adhesions in epithelial cells. EphA2 selectively inhibits cell-cell adhesions by increasing cell attachment and up-regulating the extracellular matrix protein fibronectin. The authors also show that fibronectin can contribute to important aspects of malignant character. Antibody-based targeting of EphA2 inhibits malignant cell growth by decreasing fibronectin and thereby inducing apoptotic death. These findings strengthen a concept that cancer progression is regulated by a bidirectional communication between tumor cells and their surrounding microenvironment.

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL	PG (RPG)	Referenced Work (RWK)	Referenced File
	+=====		-=====-	, +==========	, }=======
Bartley, T	1994	368	558	Nature	HCAPLUS
Carles-Kinch, K	2002	62	2840	Cancer Res	HCAPLUS
Chiarugi, P	2004	23	3905	Oncogene	HCAPLUS
Coffman, K	2003	63	7907	Cancer Res	HCAPLUS
Cunha, G	2003	107	1	Int J Cancer	HCAPLUS
D'Amico, T	2001	72	1144	Ann Thorac Surg	MEDLINE
Easty, D	1999	84	494	Int J Cancer	HCAPLUS
Fidler, I	1995	87	1588	J Natl Cancer Inst	MEDLINE
Frisch, S	1997	9	701	Curr Opin Cell Biol	HCAPLUS
Hansen, R	2000	7	95	Endocr Relat Cancer	HCAPLUS
Hayward, S	1998	13	35	Int J Oncol	HCAPLUS
Hazlehurst, L	2001	20	43	Cancer Metastasis Re	HCAPLUS
Hendrix, M	2003	22	3070	Oncogene	HCAPLUS
Hess, A	2001	61	3250	Cancer Res	HCAPLUS
Howlett, A	1995	108	1945	J Cell Sci	HCAPLUS
Huhtala, P	1995	129	867	J Cell Biol	HCAPLUS
Hunter, T	1997	88	333	Cell	HCAPLUS
Juliano, R	1994	24	118	Princess Takamatsu S	MEDLINE
Keely, P	1998	8	101	Trends Cell Biol	HCAPLUS
Kikawa, K	2002	277	39274	J Biol Chem	HCAPLUS
Kinch, M	1995	23	446	Biochem Soc Trans	HCAPLUS
Kinch, M	2003	9	613	Clin Cancer Res	HCAPLUS
Kinch, M	2003	20	59	Clin Exp Metastasis	HCAPLUS

```
Koolpe, M
                        2002
                              277
                                    46974 | J Biol Chem
                                                                 HCAPLUS
Li, L
                        1989
                                     1406
                                           J Natl Cancer Inst
                              81
                                                                 MEDLINE
                        2002
Lynch, C
                              70
                                     561
                                           Differentiation
                                                                 HCAPLUS
McCawley, L
                        2000
                              6
                                    149
                                            Mol Med Today
                                                                 HCAPLUS
                        2000
                                     62
                                           Nat Cell Biol
Miao, H
                              2
                                                                 HCAPLUS
Miao, H
                        2001
                                     527
                                            Nat Cell Biol
                              13
                                                                 HCAPLUS
Miyazaki, T
                        2003
                              103
                                     657
                                            Int J Cancer
                                                                 HCAPLUS
                        2002
Nakamoto, M
                              159
                                     58
                                            Microsc Res Tech
                                                                 HCAPLUS
                        2000
Ogawa, K
                              19
                                     6043
                                            Oncogene
                                                                 HCAPLUS
Olumi, A
                        1999
                              59
                                     5002
                                            Cancer Res
                                                                 HCAPLUS
Onn, A
                        2002
                              16
                                     423
                                            In Vivo
Park, C
                        2000
                                     324
                                            Mol Med Today
                                                                 HCAPLUS
                              6
Radinsky, R
                        1995
                              31A
                                    1091
                                            Eur J Cancer
                                                                 HCAPLUS
                        1997
                              273
                                    G824
                                            Am J Physiol
Rosenberg, I
                                                                 HCAPLUS
Ruoslahti, E
                        1999
                              76
                                            Adv Cancer Res
                                    1
                                                                 HCAPLUS
Steeg, P
                        2003
                                     55
                                            Nat Rev Cancer
                              3
                                                                 HCAPLUS
Tlsty, T
                        2001
                              11
                                     54
                                            Curr Opin Genet Dev
                                                                 HCAPLUS
Walker-Daniels, J
                        2003
                              162
                                    1037
                                            Am J Pathol
                                                                 HCAPLUS
Walker-Daniels, J
                                            Mol Cancer Res
                        2002
                              11
                                    79
                                                                 HCAPLUS
Walker-Daniels, J
                        1999
                                    275
                              41
                                            Prostate
                                                                 HCAPLUS
                                            J Mammary Gland Biol | MEDLINE
Weaver, V
                        1999
                                    193
                              4
                        2000
                                    408
Welch, D
                              12
                                            Breast Cancer Res
                                                                 HCAPLUS
                        2002
                                    599
Yu, J
                              170
                                            Differentiation
Zantek, N
                        1999
                              10
                                    629
                                            Cell Growth Differ
                                                                 HCAPLUS
Zelinski, D
                        2001
                              61
                                     2301
                                            Cancer Res
                                                                 HCAPLUS
Zeng, G
                        2003 | 163
                                    2271
                                           Am J Pathol
                                                                 HCAPLUS
```

L26 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:630173 HCAPLUS

DN 141:329420

TI EphA2 Expression Is Associated with Aggressive Features in Ovarian Carcinoma

- AU Thaker, Premal H.; Deavers, Michael; Celestino, Joseph; Thornton, Angela; Fletcher, Mavis S.; Landen, Charles N.; Kinch, Michael S.; Kiener, Peter A.; Sood, Anil K.
- CS Department of Gynecologic Oncology, the University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
- SO Clinical Cancer Research (2004), 10(15), 5145-5150 CODEN: CCREF4; ISSN: 1078-0432
- PB American Association for Cancer Research
- DT Journal
- LA English
- AB PURPOSE: EphA2 (epithelial cell kinase) is a transmembrane receptor tyrosine kinase that has been implicated in oncogenesis. There are no published data regarding the role of EphA2 in ovarian carcinoma, which is the focus of the present study. Exptl. Design: Nontransformed (HIO-180) and ovarian cancer (EG, 222, SKOV3, and A2780-PAR) cell lines were evaluated for EphA2 by Western blot anal. Five benign ovarian masses, 10 ovarian tumors of low malignant potential, and 79 invasive ovarian carcinomas were also evaluated for EphA2 expression by immunohistochem. All samples were scored in a blinded fashion. Univariate and multivariate analyses were used to determine significant assocns. between EphA2 expression and clinicopathol. variables. RESULTS: By Western blot anal., EG, 222, and SKOV3 cell lines overexpressed EphA2, whereas A2780-PAR and HIO-180 had low to absent EphA2 expression. All of the benign tumors had low or absent EphA2 expression. Among the invasive ovarian carcinomas examined (mean age of patients was 59.2 yr), 60 (75.9%) tumors overexpressed EphA2 and the other 19 tumors had neg. or minimal EphA2 expression. There was no association of EphA2 overexpression with

ascites, likelihood of nodal positivity, pathol. subtype, and optimum surgical cytoredn. (residual tumor <1 cm). However, EphA2 overexpression was significantly associated with higher tumor grade (P = 0.02) and advanced stage of disease (P = 0.001). The median survival for patients with tumor EphA2 overexpression was significantly shorter (median, 3.1 yr; P = 0.004); the median survival for patients with low or absent EphA2 tumor expression was at least 12 yr and has not yet been reached. In multivariate anal. using the Cox proportional hazards model, only volume of residual disease (P < 0.04) and EphA2 overexpression (P < 0.01) were significant and independent predictors of survival. CONCLUSIONS: EphA2 overexpression is predictive of aggressive ovarian cancer behavior and may be an important therapeutic target.

רים	В	

REIADUS	132	1 1101	l na	l p. 6	1
Referenced Author	Year			Referenced Work	Referenced
(RAU)	•	(RVL)	•	(RWK)	File
		_		+======================================	
Andres, A	1994	9	1461	Oncogene	HCAPLUS
Auersperg, N	1999	96	6249	Proc Natl Acad Sci U	HCAPLUS
Birchmeier, W	1996	213	117	Curr Top Microbiol I	HCAPLUS
Carles-Kinch, K	2002	62	2840	Cancer Res	HCAPLUS
Coffman, K	2003	63	7907	Cancer Res	HCAPLUS
Dodelet, V	2000	19	5614	Oncogene	HCAPLUS
Dohn, M	2001	20	6503	Oncogene	HCAPLUS
Drescher, U	1997	7	75	Curr Opin Neurobiol	HCAPLUS
du Bois, A	1999	10	35	Ann Oncol	1
Easty, D	2000	10	401	Melanoma Res	HCAPLUS
Flanagan, J	1998	21.	309	Annu Rev Neurosci	HCAPLUS
Flanagan, J	1997	90	403	Cell	HCAPLUS
Gale, N	1996	17	9	Neuron	HCAPLUS
Ganju, P	1994	1	1613		!
Geiger, B	!	!	<u> </u>	Oncogene	HCAPLUS
_ ·	1992	57	631	Cold Spring Harb Sym	1
Hainaut, P	2000	77	81	Adv Cancer Res	HCAPLUS
Hendrix, M	2001	98	8018	Proc Natl Acad Sci U	1
Hess, A	2001	61	3250	Cancer Res	HCAPLUS
Hess, A	2002	43	36	Proc Am Assoc Cancer	!
Hirai, H	1987	238	1717	Science (Wash DC)	HCAPLUS
Hunter, T	1992	57	25	Cold Spring Harb Sym	HCAPLUS
Jemal, A	2003	53	5	CA Cancer J Clin	
Kikawa, K	2002	277	39274	J Biol Chem	HCAPLUS
Kinch, M	1995	23	446	Biochem Soc Trans	HCAPLUS
Kinch, M	2003	20	59	Clin Exp Metastasis	HCAPLUS
Koolpe, M	2002	277	46974	J Biol Chem	HCAPLUS
Lamorte, L	2001	10	271	Surg Oncol Clin N Am	MEDLINE
Lindberg, R	1990	10	6316	Mol Cell Biol	HCAPLUS
McGuire, W	1996	334	1	N Engl J Med	HCAPLUS
Miao, H	2000	2	62	Nat Cell Biol	HCAPLUS
Miao, H	2001	İз	527	Nat Cell Biol	HCAPLUS
Miyazaki, T	2003	103	657	Int J Cancer	HCAPLUS
Nakamoto, M	2002	59	58	Microsc Res Tech	HCAPLUS
Ogawa, K	2000	19	6043	Oncogene	HCAPLUS
Orioli, D	1997	13	354	Trends Genet	HCAPLUS
Pandey, A	1994	269	30154	J Biol Chem	HCAPLUS
Pandey, A	1995	270	19201	J Biol Chem	HCAPLUS
Pandey, A	1995	268	567	Science (Wash DC)	HCAPLUS
Pejovic, T	1995	27	73	Ann Med	!
-	:	!	! -		MEDLINE
Pratt, R	2002	21	7690	Oncogene	HCAPLUS
Rosenberg, I	1997	273	G824	Am J Physiol	HCAPLUS
Sood, A	2001	158	1279	Am J Pathol	HCAPLUS
Sood, A	2002	1	661	Cancer Biol Ther	l

Sood, A	1999	5	2485	Clin Cancer Res	HCAPLUS
Sood, A	2002	9	2	J Soc Gyn Invest	Ì
Straume, O	2002	160	1009.	Am J Pathol	HCAPLUS
Sultan, E	1997	40	371	Genomics	
Vousden, K	2002	1602	47	Biochem Biophys Acta	HCAPLUS
Walker-Daniels, J	2003	162	1037	Am J Pathol	HCAPLUS
Walker-Daniels, J	2002	1	79	Mol Cancer Res	HCAPLUS
Walker-Daniels, J	1999	41	275	Prostate	HCAPLUS
Zantek, N	1999	10	629	Cell Growth Differ	HCAPLUS
Zeliniski, D	2001	61	2301	Cancer Res	İ
Zetter, B	1993	4	219	Semin Cancer Biol	HCAPLUS

=> => fil medline

FILE 'MEDLINE' ENTERED AT 12:31:34 ON 07 JUL 2005

FILE LAST UPDATED: 6 JUL 2005 (20050706/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/

http://www.nlm.nih.gov/pubs/techbull/nd04/nd04 mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

- L52 ANSWER 1 OF 11 MEDLINE on STN
- AN 2003596894 MEDLINE
- DN PubMed ID: 14679012
- TI **EphA2** as target of anticancer immunotherapy: identification of HLA-A*0201-restricted epitopes.
- AU Alves Pedro M S; Faure Olivier; Graff-Dubois Stephanie; Gross David-Alexandre; Cornet Sebastien; Chouaib Salem; Miconnet Isabelle; Lemonnier Francois A; Kosmatopoulos Kostas
- CS INSERM487, Institut Gustave Roussy, Villejuif. Unite d'Immunite Cellulaire Antivirale, Institut Pasteur, Paris. Immuno-Designed Molecules, Paris, France.
- SO Cancer research, (2003 Dec 1) 63 (23) 8476-80. Journal code: 2984705R. ISSN: 0008-5472.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 200402
- ED Entered STN: 20031218

Last Updated on STN: 20040302

Entered Medline: 20040227

AB **EphA2** (Eck) is a tyrosine kinase receptor that is overexpressed in several human cancers such as breast, colon, lung, prostate, gastric carcinoma, and metastatic melanoma but not in nonmalignant counterparts.

```
To validate EphA2 as a tumor antigen recognized by CD8+ T
     lymphocytes, we used reverse immunology approach to identify
     HLA-A*0201-restricted epitopes. Peptides bearing the HLA-A*0201-specific
     anchor motifs were analyzed for their capacity to bind and stabilize the
     HLA-A*0201 molecules. Two peptides, EphA2(58) and EphA2
     (550), with a high affinity for HLA-A*0201 were selected. Both peptides
     were immunogenic in the HLA-A*0201-transgenic HHD mice. Interestingly,
     peptide-specific murine CTLs cell lines responded to COS-7 cells
     coexpressing HLA-A*0201 and EphA2 and to EphA2
     -positive human tumor cells of various origin (renal cell, lung, and colon
     carcinoma and sarcoma). This demonstrates that EphA2 (58) and
     EphA2 (550) are naturally processed from endogenous EphA2
        In addition, EphA2(58) and EphA2(550) stimulated
     specific CD8(+) T cells from healthy donor peripheral blood mononuclear
     cells. These T cells recognized EphA2-positive human tumor
     cells in an HLA-A*0201-restricted manner. Interestingly, EphA2
     -specific CD8+ T cells were detected in the peripheral blood mononuclear
     cells of prostate cancer patients. These results show for the first time
     that EphA2 is a tumor rejection antigen and lead us to propose
     EphA2(58) and EphA2(550) peptides for a
     broad-spectrum-tumor immunotherapy.
      Animals
      CD8-Positive T-Lymphocytes: IM, immunology
      COS Cells
      Cell Line, Tumor
      Cercopithecus aethiops
      Epitope Mapping
      Epitopes, T-Lymphocyte: IM, immunology
     *HLA-A Antigens: IM, immunology
     *Immunotherapy: MT, methods
      Lymphocyte Activation: IM, immunology
      Mice
      Mice, Transgenic
      Neoplasms: EN, enzymology
      Neoplasms: IM, immunology
     *Neoplasms: TH, therapy
     *Peptide Fragments: IM, immunology
      Peptide Fragments: PD, pharmacology
       *Receptor, EphA2: IM, immunology
      Research Support, Non-U.S. Gov't
      T-Lymphocytes, Cytotoxic: IM, immunology
     0 (Epitopes, T-Lymphocyte); 0 (HLA-A Antigens); 0 (HLA-A*0201 antigen); 0
     (Peptide Fragments); EC 2.7.1.112 (Receptor, EphA2)
L52 ANSWER 2 OF 11
                        MEDLINE on STN
     2003282791
                    MEDLINE
     PubMed ID: 12810680
     EphA2 overexpression decreases estrogen dependence and tamoxifen
     sensitivity.
     Lu Ming; Miller Kathy D; Gokmen-Polar Yesim; Jeng Meei-Huey; Kinch Michael
     Department of Basic Medical Sciences, Purdue University Cancer Center,
     West Lafayette, Indiana 47907, USA.
     CA91318 (NCI)
     Cancer research, (2003 Jun 15) 63 (12) 3425-9.
     Journal code: 2984705R. ISSN: 0008-5472.
     United States
     Journal; Article; (JOURNAL ARTICLE)
     English
     Priority Journals
```

CT

CN

AN

DN

TI

ΑU

CS

NC

SO

CY

DT LA

FS

```
EΜ
     200307
ED
     Entered STN: 20030618
     Last Updated on STN: 20030729
     Entered Medline: 20030728
AB
     The EphA2 receptor tyrosine kinase is found at low levels on
     nontransformed adult breast epithelial cells but is frequently
     overexpressed on aggressive breast cancer cells. Recent studies have
     documented an inverse relationship between EphA2 and estrogen
     receptor expression in breast cancer cell lines. In our present study, we
     demonstrate that overexpression of EphA2 decreases estrogen
     dependence as defined using both in vitro and in vivo criteria.
     EphA2-transfected cells demonstrate increased growth in vitro and
     form larger and more aggressive tumors in vivo. EphA2
     overexpression also decreases the ability of tamoxifen to inhibit breast
     cancer cell growth and tumorigenesis. These effects of EphA2
     overexpression can be overcome by antibody-based targeting of
     EphA2. In particular, certain EphA2 antibodies can
     resensitize EphA2-overexpressing breast tumor cells to
     tamoxifen. These results have important implications for understanding
     the molecular basis underlying estrogen dependence and provide further
     evidence that EphA2 may provide a much-needed therapeutic target
     for breast cancer.
     Check Tags: Female
      Adenocarcinoma: ME, metabolism
     *Adenocarcinoma: PA, pathology
      Animals
      Antibodies, Monoclonal: PD, pharmacology
     *Antineoplastic Agents, Hormonal: PD, pharmacology
      Breast Neoplasms: ME, metabolism
     *Breast Neoplasms: PA, pathology
     *Drug Resistance, Neoplasm
      Estradiol: PD, pharmacology
     *Estrogen Receptor Modulators: PD, pharmacology
     *Estrogens
      Genes, Reporter
      Humans
      Mice
      Mice, Nude
      Neoplasm Invasiveness
     *Neoplasm Proteins: ME, metabolism
      Neoplasm Transplantation
      Neoplasms, Hormone-Dependent: ME, metabolism
     *Neoplasms, Hormone-Dependent: PA, pathology
        Receptor, EphA2: AI, antagonists & inhibitors
        Receptor, EphA2: GE, genetics
        Receptor, EphA2: IM, immunology
       *Receptor, EphA2: PH, physiology
     *Receptors, Estrogen: ME, metabolism
      Recombinant Fusion Proteins: PH, physiology
      Research Support, Non-U.S. Gov't
      Research Support, U.S. Gov't, Non-P.H.S.
      Research Support, U.S. Gov't, P.H.S.
      Stress
     *Tamoxifen: PD, pharmacology
      Tumor Cells, Cultured: ME, metabolism
      Tumor Cells, Cultured: PA, pathology
      Xenograft Model Antitumor Assays
RN
     10540-29-1 (Tamoxifen); 50-28-2 (Estradiol)
     0 (Antibodies, Monoclonal); 0 (Antineoplastic Agents, Hormonal); 0
```

(Estrogen Receptor Modulators); 0 (Estrogens); 0 (Neoplasm Proteins); 0

```
(Receptors, Estrogen); 0 (Recombinant Fusion Proteins); EC 2.7.1.112
     (Receptor, EphA2)
L52 ANSWER 3 OF 11
                        MEDLINE on STN
     2003136340
                    MEDLINE
     PubMed ID: 12651595
DN
ΤI
     Differential regulation of EphA2 in normal and malignant cells.
     Walker-Daniels Jennifer; Hess Angela R; Hendrix Mary J C; Kinch Michael S
AU
     Department of Basic Medical Sciences, Purdue University Cancer Center,
CS
     West Lafayette, Indiana, USA.
NC
     1 R21 CA85615 (NCI)
     2 R37 CA59702 (NCI)
     2 T32 CA79445-03 (NCI)
     American journal of pathology, (2003 Apr) 162 (4) 1037-42. Ref:
SO
     Journal code: 0370502. ISSN: 0002-9440.
CY
     United States
DT
     Journal; Article; (JOURNAL ARTICLE)
     General Review; (REVIEW)
     (REVIEW, TUTORIAL)
LA
     English
FS
     Abridged Index Medicus Journals; Priority Journals
EΜ
     200306
     Entered STN: 20030325
     Last Updated on STN: 20030613
     Entered Medline: 20030612
CT
     *Gene Expression Regulation: PH, physiology
     *Gene Expression Regulation, Neoplastic: PH, physiology
     Humans
     *Neoplasms: GE, genetics
     *Neoplasms: PA, pathology
       *Receptor, EphA2: GE, genetics
      Reference Values
      Research Support, U.S. Gov't, Non-P.H.S.
      Research Support, U.S. Gov't, P.H.S.
      Signal Transduction
     EC 2.7.1.112 (Receptor, EphA2)
CN
L52 ANSWER 4 OF 11
                        MEDLINE on STN
AN
     2003135956
                    MEDLINE
DN
     PubMed ID: 12650608
     Overexpression and functional alterations of the EphA2 tyrosine
TI
     kinase in cancer.
AU
     Kinch Michael S; Carles-Kinch Kelly
    MedImmune, Inc., Gaithersburg, Maryland 20878, USA.. kinchm@medimmune.com
CS
SO
     Clinical & experimental metastasis, (2003) 20 (1) 59-68. Ref:
     Journal code: 8409970. ISSN: 0262-0898.
CY
    Netherlands
DΤ
     Journal; Article; (JOURNAL ARTICLE)
     General Review; (REVIEW)
     (REVIEW, TUTORIAL)
     English
LA
FS
     Priority Journals
EM
     200303
     Entered STN: 20030325
ED
     Last Updated on STN: 20030401
     Entered Medline: 20030331
AB
     Cancer is a disease of aberrant signal transduction. The expression and
     function of intracellular signaling pathways are frequently subverted as
```

cells progress towards a metastatic phenotype. In particular, tyrosine kinases initiate powerful signals that govern many different aspects of cell behavior. In Recent studies have demonstrated that the EphA2 receptor tyrosine kinase is frequently overexpressed and functionally altered in aggressive tumor cells, and that these changes promote metastatic character. Herein, we provide an overview of our current understanding of EphA2, with emphasis upon the differential regulation of EphA2 expression and function. We also show that differential EphA2 expression and function may provide a unique opportunity for selective therapeutic targeting of EphA2 in metastatic disease.

Gene Expression Regulation, Neoplastic Humans
Models, Biological
Neoplasm Metastasis
Neoplasms: GE, genetics
*Neoplasms: ME, metabolism
Neoplasms: PA, pathology
Nervous System: EM, embryology
Nervous System: EN, enzymology

Nervous System: GD, growth & development

Receptor, EphA2: GE, genetics *Receptor, EphA2: ME, metabolism Receptor, EphA2: PH, physiology

CN EC 2.7.1.112 (Receptor, EphA2)

L52 ANSWER 5 OF 11 MEDLINE on STN

AN 2003066115 MEDLINE

DN PubMed ID: 12576426

- TI Predictive value of the EphA2 receptor tyrosine kinase in lung cancer recurrence and survival.
- AU Kinch Michael S; Moore Mary-Beth; Harpole David H Jr
- CS MedImmune, Inc., Gaithersburg, Maryland 20878, USA.
- SO Clinical cancer research: an official journal of the American Association for Cancer Research, (2003 Feb) 9 (2) 613-8.

 Journal code: 9502500. ISSN: 1078-0432.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 200308
- ED Entered STN: 20030211 Last Updated on STN: 20030802

Entered Medline: 20030801

AB PURPOSE: Underestimation of disease severity is a major problem confronting the successful clinical management of non-small cell lung cancer. Recent advances in molecular biological substaging may provide an opportunity to identify those patients with the most aggressive forms of the disease, but there is a continuing need for accurate markers of disease relapse and survival. EXPERIMENTAL DESIGN: In our present study, immunohistochemical analyses of a retrospective database of pathologic specimens were used to demonstrate that the EphA2 receptor kinase is frequently overexpressed in NSCLC. RESULTS: Initial presentation with high levels of EphA2 predicts subsequent survival, overall relapse, and site of relapse. Specifically, high levels of EphA2 in the primary tumor predict brain metastases, whereas low levels of EphA2 relate to disease-free survival or

contralateral lung metastasis. CONCLUSIONS: These data suggest that **EphA2** may provide a molecular marker to identify and predict patients who have isolated brain metastases. Moreover, the high levels of

```
EphA2 in lung cancer may provide an opportunity for therapeutic
     targeting.
     Check Tags: Female; Male
      Brain Neoplasms: PA, pathology
      Brain Neoplasms: SC, secondary
      Carcinoma, Non-Small-Cell Lung: MO, mortality
     *Carcinoma, Non-Small-Cell Lung: PA, pathology
      Disease-Free Survival
      Humans
      Immunohistochemistry
      Lung Neoplasms: MO, mortality
     *Lung Neoplasms: PA, pathology
      Lung Neoplasms: SC, secondary
      Middle Aged
      Neoplasm Metastasis
      Neoplasm Staging
      Predictive Value of Tests
       *Receptor, EphA2: ME, metabolism
      Recurrence
      Survival Analysis
      Survival Rate
      Time Factors
      Tumor Markers, Biological: ME, metabolism
     0 (Tumor Markers, Biological); EC 2.7.1.112 (Receptor, EphA2)
    ANSWER 6 OF 11
                        MEDLINE on STN
                    MEDLINE
ΑN
     2002734145
DN
     PubMed ID: 12496364
TΤ
     Blockade of EphA receptor tyrosine kinase activation inhibits vascular
     endothelial cell growth factor-induced angiogenesis.
     Cheng Nikki; Brantley Dana M; Liu Hua; Lin Qin; Enriquez Miriam; Gale
AU
     Nick; Yancopoulos George; Cerretti Douglas Pat; Daniel Thomas O; Chen Jin
     Department of Cancer Biology, Medicine, Vanderbilt University School of
CS
     Medicine, Nashville, TN 37232, USA.
NC
     DK47078 (NIDDK)
     HD36400 (NICHD)
     P30CA68485 (NCI)
     T-32 CA09592 (NCI)
     T32-HL-07751-06 (NHLBI)
     Molecular cancer research : MCR, (2002 Nov) 1 (1) 2-11.
     Journal code: 101150042. ISSN: 1541-7786.
CY
     United States
DT
     Journal; Article; (JOURNAL ARTICLE)
LA
     English
FS
     Priority Journals
EΜ
     200306
     Entered STN: 20021227
     Last Updated on STN: 20030612
     Entered Medline: 20030611
     Angiogenesis is a multistep process involving a diverse array of molecular
     signals. Ligands for receptor tyrosine kinases (RTKs) have emerged as
     critical mediators of angiogenesis. Three families of ligands, vascular
     endothelial cell growth factors (VEGFs), angiopoietins, and ephrins, act
     via RTKs expressed in endothelial cells. Recent evidence indicates that
     VEGF cooperates with angiopoietins to regulate vascular remodeling and
     angiogenesis in both embryogenesis and tumor neovascularization. However,
     the relationship between VEGF and ephrins remains unclear. Here we show
     that interaction between EphA RTKs and ephrinA ligands is necessary for
     induction of maximal neovascularization by VEGF. EphA2 RTK is
     activated by VEGF through induction of ephrinAl ligand. A soluble
```

```
EphA2-Fc receptor inhibits VEGF-, but not basic fibroblast growth
     factor-induced endothelial cell survival, migration, sprouting, and
     corneal angiogenesis. As an independent, but complementary approach,
     EphA2 antisense oligonucleotides inhibited endothelial expression
     of EphA2 receptor and suppressed ephrinA1- and VEGF-induced cell
     migration. Taken together, these data indicate an essential role for EphA
     receptor activation in VEGF-dependent angiogenesis and suggest a potential
     new target for therapeutic intervention in pathogenic angiogenesis.
     *Angiogenesis Inhibitors: PD, pharmacology
     Animals
     Apoptosis: DE, drug effects
      Cell Division: DE, drug effects
      Cell Movement: DE, drug effects
      Cell Survival: DE, drug effects
      Cells, Cultured
      Corneal Neovascularization
     *Endothelial Growth Factors: AI, antagonists & inhibitors
     Endothelium, Vascular: CY, cytology
     *Endothelium, Vascular: DE, drug effects
     Endothelium, Vascular: PH, physiology
     *Enzyme Activation: PH, physiology
      Ephrin-A1: ME, metabolism
      Ephrin-A1: PD, pharmacology
      Fibroblast Growth Factor 2: PD, pharmacology
      Intercellular Signaling Peptides and Proteins
     *Lymphokines: AI, antagonists & inhibitors
     Mice
     Mice, Inbred C57BL
     *Neovascularization, Physiologic: DE, drug effects
      Oligonucleotides, Antisense: PD, pharmacology
      Phosphorylation
       *Receptor, EphA2: AI, antagonists & inhibitors
       Receptor, EphA2: ME, metabolism
      Research Support, Non-U.S. Gov't
      Research Support, U.S. Gov't, P.H.S.
     Umbilical Veins: CY, cytology
      Vascular Endothelial Growth Factor A
      Vascular Endothelial Growth Factors
     103107-01-3 (Fibroblast Growth Factor 2)
     0 (Angiogenesis Inhibitors); 0 (Endothelial Growth Factors); 0
     (Ephrin-A1); 0 (Intercellular Signaling Peptides and Proteins); 0
     (Lymphokines); 0 (Oligonucleotides, Antisense); 0 (Vascular Endothelial
     Growth Factor A); 0 (Vascular Endothelial Growth Factors); EC 2.7.1.112
     (Receptor, EphA2)
L52 ANSWER 7 OF 11
                        MEDLINE on STN
     2002730653
                    MEDLINE
     PubMed ID: 12494475
     EphA2 overexpression correlates with poor prognosis in
     esophageal squamous cell carcinoma.
     Miyazaki Tatsuya; Kato Hiroyuki; Fukuchi Minoru; Nakajima Masanobu; Kuwano
     Hiroyuki
     Department of Surgery I, Gunma University Faculty of Medicine, Gunma,
     Japan.. tatsuyam@showa.gunma-u.ac.jp
     International journal of cancer. Journal international du cancer,
     (2003 Feb 20) 103 (5) 657-63.
     Journal code: 0042124. ISSN: 0020-7136.
     United States
     Journal; Article; (JOURNAL ARTICLE)
```

RN

CN

AN

DN

ΤI

ΑU

CS

SO

CY

DT

```
LΑ
    English
FS
    Priority Journals
EΜ
     200302
ED
    Entered STN: 20021221
    Last Updated on STN: 20030207
     Entered Medline: 20030206
    EphA2 is a member of the Eph family of receptor tyrosine
    kinases, which interact with cell-bound ligands known as ephrins.
     EphA2 expression was investigated by immunohistochemistry with an
     anti-EphA2 monoclonal antibody in 80 patients with esophageal
     squamous cell carcinoma (ESCC) who had undergone surgery. EphA2
     overexpression was positive in 40 of the 80 patients (50%). A significant
     correlation was observed between EphA2 expression and regional
     lymph node metastasis (p=0.023), number of lymph node metastases (p=0.011)
     and poor degree of tumor differentiation (p=0.004). The survival rates of
     EphA2-positive patients were poorer than those of EphA2
     -negative patients (p=0.014). The 5-year survival rate of patients
     without EphA2 overexpression was 68%, whereas that of patients
     with EphA2 overexpression was 29%. EphA2 expression
     was also investigated in 7 ESCC cell lines (TE-1, -2, -8, -13, -15, TT and
     TTn) and 1 immortalized human esophageal keratinocyte cell line (CHEK-1).
     Western blotting revealed different levels of EphA2 expression
     in the 8 cell lines. EphA2 was expressed at a high level in the
     ESCC cell lines compared to CHEK-1. EphA2 phosphorylation was
     demonstrated in all cell lines. Northern blot analysis showed that
     EphA2 mRNA expression in TE-1 was greater than that in the other
     ESCC cell lines. The observation of small gaps on Western blot analysis
     of the ESCC cell lines suggests that there may be a mechanism for
    EphA2 regulation at the point of translation. In conclusion,
    EphA2 overexpression appears to be related to poor degree of tumor
    differentiation and lymph node metastasis in ESCC. Consequently, patients
    with EphA2 overexpression have a poorer prognosis than those
    without. EphA2 is a potential target to prevent ESCC cells
     spreading into the lymphatic drainage.
     Copyright 2002 Wiley-Liss, Inc.
CT
     Check Tags: Comparative Study; Female; Male
     Adult
     Aged
     Blotting, Northern
     Blotting, Western
     *Carcinoma, Squamous Cell: GE, genetics
     Carcinoma, Squamous Cell: ME, metabolism
     Carcinoma, Squamous Cell: SC, secondary
     Cysteine Proteinase Inhibitors: PD, pharmacology
     DNA, Neoplasm: AN, analysis
     Ephrin-A1: ME, metabolism
     Ephrin-A1: PD, pharmacology
     *Esophageal Neoplasms: GE, genetics
     Esophageal Neoplasms: ME, metabolism
     Esophageal Neoplasms: PA, pathology
     Gene Expression Regulation, Neoplastic
     Humans
     Immunoenzyme Techniques
     Leupeptins: PD, pharmacology
     Lymphatic Metastasis: GE, genetics
     Middle Aged
     Mutation
     Phosphorylation
     Prognosis
```

Protein-Tyrosine Kinase: ME, metabolism

```
RNA, Neoplasm: ME, metabolism
       Receptor, EphA2: GE, genetics
       *Receptor, EphA2: ME, metabolism
      Survival Rate
      Tumor Cells, Cultured
RN
     133407-82-6 (benzyloxycarbonylleucyl-leucyl-leucine aldehyde)
CN
     0 (Cysteine Proteinase Inhibitors); 0 (DNA, Neoplasm); 0 (Ephrin-A1); 0
     (Leupeptins); 0 (RNA, Neoplasm); EC 2.7.1.112 (Protein-Tyrosine Kinase);
     EC 2.7.1.112 (Receptor, EphA2); EC 2.7.1.112 (focal adhesion
     kinase)
L52 ANSWER 8 OF 11
                        MEDLINE on STN
     2002696033
                    MEDLINE
AN
DN
     PubMed ID: 12351647
ΤI
     An ephrin mimetic peptide that selectively targets the EphA2
ΑU
     Koolpe Mitchell; Dail Monique; Pasquale Elena B
CS
     Burnham Institute, La Jolla, California 92037, USA.
NC
     CA82713 (NCI)
SO
     Journal of biological chemistry, (2002 Dec 6) 277 (49) 46974-9.
     Electronic Publication: 2002-09-25.
     Journal code: 2985121R. ISSN: 0021-9258.
CY
     United States
DT
     Journal; Article; (JOURNAL ARTICLE)
     English
LA
FS
     Priority Journals
EΜ
     200302
ED
     Entered STN: 20021217
     Last Updated on STN: 20030205
     Entered Medline: 20030204
     Eph receptor tyrosine kinases represent promising disease targets because
     they are differentially expressed in pathologic versus normal tissues.
     The EphA2 receptor is up-regulated in transformed cells and
     tumor vasculature where it likely contributes to cancer pathogenesis.
     exploit EphA2 as a therapeutic target, we used phage display to
     identify two related peptides that bind selectively to EphA2
     with high affinity (submicromolar K(D) values). The peptides target the
     ligand-binding domain of EphA2 and compete with ephrin ligands
     for binding. Remarkably, one of the peptides has ephrin-like activity in
     that it stimulates EphA2 tyrosine phosphorylation and signaling.
     Furthermore, this peptide can deliver phage particles to endothelial and
     tumor cells expressing EphA2. In contrast, peptides
     corresponding to receptor-interacting portions of ephrin ligands bind
     weakly and promiscuously to many Eph receptors. Bioactive ephrin mimetic
     peptides could be used to selectively deliver agents to Eph
     receptor-expressing tissues and modify Eph signaling in therapies for
     cancer, pathological angiogenesis, and nerve regeneration.
CT
     Amino Acid Sequence
     Dose-Response Relationship, Drug
      Endothelium, Vascular: CY, cytology
      Enzyme-Linked Immunosorbent Assay
     *Ephrins: CH, chemistry
     Humans
     Hydrogen-Ion Concentration
      Immunoblotting
      Kinetics
     Ligands
     Molecular Sequence Data
      Peptides: CH, chemistry
      Phosphorylation
```

```
Plasmids: ME, metabolism
      Precipitin Tests
      Protein Binding
      Protein Structure, Tertiary
      Protein-Tyrosine Kinase: ME, metabolism
       *Receptor, EphA2: CH, chemistry
        Receptor, EphA2: ME, metabolism
      Research Support, Non-U.S. Gov't
      Research Support, U.S. Gov't, Non-P.H.S.
      Research Support, U.S. Gov't, P.H.S.
      Sequence Homology, Amino Acid
      Signal Transduction
      Tyrosine: ME, metabolism
      Umbilical Veins: ME, metabolism
RN
     55520-40-6 (Tyrosine)
CN
     0 (Ephrins); 0 (Ligands); 0 (Peptides); 0 (Plasmids); EC 2.7.1.112
     (Protein-Tyrosine Kinase); EC 2.7.1.112 (Receptor, EphA2)
     ANSWER 9 OF 11
L52
                        MEDLINE on STN
AN
     2002398166
                   MEDLINE
DN
     PubMed ID: 12147253
TI
     Negative regulation of EphA2 receptor by Cbl.
AU
     Wang You jie; Ota Satoshi; Kataoka Hideki; Kanamori Masao; Li Zhong you;
     Band Hamid; Tanaka Masamitsu; Sugimura Haruhiko
CS
     First Department of Pathology, Hamamatsu University School of Medicine,
     1-20-1, Handayama, 431-3192, Hamamatsu, Japan.
NC
     CA75075 (NCI)
     CA76118 (NCI)
     CA87986 (NCI)
SO
     Biochemical and biophysical research communications, (2002 Aug 9)
     296 (1) 214-20.
     Journal code: 0372516. ISSN: 0006-291X.
CY
     United States
DT
     Journal; Article; (JOURNAL ARTICLE)
LA
     English
FS
     Priority Journals
EM
     200209
ED
     Entered STN: 20020731
     Last Updated on STN: 20020907
     Entered Medline: 20020906
AB
     The c-Cbl proto-oncogene product Cbl has emerged as a negative regulator
     of receptor and non-receptor tyrosine kinases, a function dependent on its
     recently identified ubiquitin ligase activity. Here, we report that
     EphA2, a member of Eph receptor tyrosine kinases is negatively
     regulated by Cbl. The negative regulation of EphA2 mediated by
     Cbl is dependent on the activity of EphA2, as the kinase
     inactive mutant of EphA2 cannot be regulated by Cbl. Moreover,
     a point mutation (G306E-Cbl) in TKB region of Cbl that has been reported
     to abolish Cbl binding to RTKs and non-receptor tyrosine kinases impaired
     the binding to active EphA2. The dominant negative mutant
     70Z-Cbl, which has a 17-amino acids deletion in the N-boundary of the RING
     finger domain, defuncted negative regulatory function of Cbl to
     EphA2. These results demonstrate that the TKB domain and RING
     finger domain of Cbl are essential for this negative regulation.
CT
      Cell Line
      Humans
      Phosphorylation
      Receptor Protein-Tyrosine Kinases: ME, metabolism
     *Receptor Protein-Tyrosine Kinases: PH, physiology
        Receptor, EphA2
```

```
Research Support, Non-U.S. Gov't
      Research Support, U.S. Gov't, Non-P.H.S.
      Research Support, U.S. Gov't, P.H.S.
     *Retroviridae Proteins, Oncogenic: PH, physiology
CN
     0 (Retroviridae Proteins, Oncogenic); 0 (oncogene protein v-cbl); EC
     2.7.1.112 (Receptor Protein-Tyrosine Kinases); EC 2.7.1.112 (Receptor,
     EphA2)
     ANSWER 10 OF 11
L52
                         MEDLINE on STN
     2002279542
                    MEDLINE
AN
DN
     PubMed ID: 12019162
TΙ
     Antibody targeting of the EphA2 tyrosine kinase inhibits
     malignant cell behavior.
IIA
     Carles-Kinch Kelly; Kilpatrick Katherine E; Stewart Jane C; Kinch Michael
CS
     Department of Basic Medical Science, Purdue University Cancer Center, West
     Lafayette, Indiana 47907, USA.
NC
     1U01 CA 91318 (NCI)
SO
     Cancer research, (2002 May 15) 62 (10) 2840-7.
     Journal code: 2984705R. ISSN: 0008-5472.
CY
     United States
\mathtt{DT}
     Journal; Article; (JOURNAL ARTICLE)
LA
     English
FS
     Priority Journals
EM
     200207
ED
     Entered STN: 20020522
     Last Updated on STN: 20020712
     Entered Medline: 20020710
AB
     EphA2 is a transmembrane receptor tyrosine kinase that is
     up-regulated on many aggressive carcinoma cells. Despite its
     overexpression, the EphA2 on malignant cells fails to bind its
     ligand, ephrinA1, which is anchored to the membrane of adjacent cells.
     Unlike other receptor kinases, EphA2 demonstrates kinase
     activity that is independent of ligand binding. However, ligand binding
     causes EphA2 to negatively regulate tumor cell growth and
     migration. Herein, we translate knowledge of EphA2 into
     strategies that selectively target malignant cells. Using a novel
     approach to preserve extracellular epitopes and optimize antibody
     diversity, we generated monoclonal antibodies that identify epitopes on
     the extracellular domain of EphA2. EphA2 antibodies
     were selected for their abilities to inhibit behaviors that are unique to
     metastatic cells while minimizing damage to nontransformed cells. A
     subset of EphA2 monoclonal antibodies were found to inhibit the
     soft agar colonization by MDA-MB-231 breast tumor cells but did not affect
     monolayer growth by nontransformed MCF-10A breast epithelial cells. These
     EphA2 antibodies also prevented tumor cells from forming tubular
     networks on reconstituted basement membranes, which is a sensitive
     indicator of metastatic character. Biochemical analyses showed that
     biologically active antibodies induced EphA2 phosphorylation and
     subsequent degradation. Antisense-based targeting of EphA2
     similarly inhibited soft agar colonization, suggesting that the antibodies
     repress malignant behavior by down-regulating EphA2. These
     results suggest an opportunity for antibody-based targeting of the many
     cancers that overexpress EphA2. Our studies also emphasize how
     tumor-specific cellular behaviors can be exploited to identify and screen
     potential therapeutic targets.
CT
     Check Tags: Female; Male
     *Antibodies, Monoclonal: IM, immunology
      Antibodies, Monoclonal: IP, isolation & purification
```

Antibodies, Monoclonal: PD, pharmacology

```
Breast Neoplasms: EN, enzymology
     *Breast Neoplasms: PA, pathology
      Breast Neoplasms: TH, therapy
      Cell Division: DE, drug effects
      Collagen
      Drug Combinations
      Epithelial Cells: CY, cytology
      Epithelial Cells: DE, drug effects
      Epithelial Cells: ME, metabolism
      Epitopes: IM, immunology
      Growth Inhibitors: IM, immunology
      Growth Inhibitors: PD, pharmacology
      Humans
      Immunization, Passive: MT, methods
      Laminin
      Prostatic Neoplasms: EN, enzymology
     *Prostatic Neoplasms: PA, pathology
      Prostatic Neoplasms: TH, therapy
      Proteoglycans
     *Receptor Protein-Tyrosine Kinases: AI, antagonists & inhibitors
     *Receptor Protein-Tyrosine Kinases: IM, immunology
      Receptor Protein-Tyrosine Kinases: ME, metabolism
        Receptor, EphA2
      Research Support, U.S. Gov't, Non-P.H.S.
      Research Support, U.S. Gov't, P.H.S.
      Tumor Cells, Cultured
RN
     119978-18-6 (matrigel); 9007-34-5 (Collagen)
CN
     0 (Antibodies, Monoclonal); 0 (Drug Combinations); 0 (Epitopes); 0 (Growth
     Inhibitors); 0 (Laminin); 0 (Proteoglycans); EC 2.7.1.112 (Receptor
     Protein-Tyrosine Kinases); EC 2.7.1.112 (Receptor, EphA2)
L52 ANSWER 11 OF 11
                         MEDLINE on STN
AN
     96243041
                 MEDLINE
DN
     PubMed ID: 8649815
TI
     Germ-line inactivation of the murine Eck receptor
     tyrosine kinase by gene trap retroviral insertion.
ΑU
     Chen J; Nachabah A; Scherer C; Ganju P; Reith A; Bronson R; Ruley H E
CS
     Department of Microbiology and Immunology, Vanderbilt University School of
     Medicine, Nashville, Tennessee 37232, USA.
NC
     1 F32 GM17003-01 (NIGMS)
     RO1GM84688 (NIGMS)
SO
     Oncogene, (1996 Mar 7) 12 (5) 979-88.
     Journal code: 8711562. ISSN: 0950-9232.
CY
     ENGLAND: United Kingdom
DT
     Journal; Article; (JOURNAL ARTICLE)
LA
     English
     Priority Journals
FS
     GENBANK-U28385
os
ΕM
     199607
ED
     Entered STN: 19960805
     Last Updated on STN: 20000303
     Entered Medline: 19960722
AB
     The present study characterized a mutation in the Eck
     receptor tyrosine kinase gene induced by the
     U3betageo gene trap retrovirus. The mutation (eck(i)) was identified
     during an in vitro screen for proviruses that disrupt developmentally
     regulated genes in cultured ES cells. The germ-line eck(i) fusion gene
     was expressed in blastocyst and later restricted to the primitive streak,
     node and to regions of the hindbrain in 6.5-10.5 day embryos. This is
     identical to the pattern of Eck gene expression as determined by either in
```

situ hybridization or immunostaining, suggesting that expression of the Eck promoter was not affected by provirus integration. The provirus inserted approximately 8 kb upstream of the 5' end of the published cDNA sequence, and 1.8 kb downstream of an alternatively spliced 5' exon. eck(i) allele is essentially a null mutation since mutant mice are severely deficient for Eck protein as determined by Western blot analysis and in vitro kinase assays. Nevertheless, mice homozygous for the mutation did not exhibit any discernable phenotype. These results suggest that other members of the Eph family of receptor tyrosine kinases can functionally compensate for loss of Eck.

CTCheck Tags: Female; Male Animals Base Sequence Blastocyst

*Exons: GE, genetics

*Genes, Structural: GE, genetics

*Genetic Vectors: GE, genetics

Homozygote

Membrane Proteins: DF, deficiency *Membrane Proteins: GE, genetics

Mice

Mice, Inbred C57BL

Molecular Sequence Data

*Mutagenesis, Insertional: GE, genetics Mutagenesis, Insertional: MT, methods Phenotype

*Proviruses: GE, genetics

*Receptor Protein-Tyrosine Kinases: GE, genetics Receptor Protein-Tyrosine Kinases: ME, metabolism

Receptor, EphA2

Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.

*Restriction Mapping

Rhombencephalon: EM, embryology

Rhombencephalon: ME, metabolism

CN 0 (Genetic Vectors); 0 (Membrane Proteins); EC 2.7.1.112 (Receptor Protein-Tyrosine Kinases); EC 2.7.1.112 (Receptor, EphA2)

=> => fil biosis FILE 'BIOSIS' ENTERED AT 12:35:37 ON 07 JUL 2005 Copyright (c) 2005 The Thomson Corporation

FILE COVERS 1969 TO DATE. CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 29 June 2005 (20050629/ED)

FILE RELOADED: 19 October 2003.

=> d all tot

ANSWER 1 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN L59 AN2004:123940 BIOSIS

DN PREV200400127027

Expression, purification, and initial characterization of the cytoplasmic TI domains of the human receptor tyrosine kinase, EphA2.

AU Zabell, Kathryn M. [Reprint Author]; Kinch, Michael S.; Knapp, Deborah W.; Stauffacher, Cynthia V. [Reprint Author]

```
CS
     Biological Sciences, Purdue University, Lafayette, IN, USA
SO
     Biophysical Journal, (January 2004) Vol. 86, No. 1, pp. 254a. print.
     Meeting Info.: 48th Annual Meeting of the Biophysical Society.
     Baltimore, MD, USA. February 14-18, 2004. Biophysical Society.
     ISSN: 0006-3495 (ISSN print).
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LΑ
     English
ED
     Entered STN: 3 Mar 2004
     Last Updated on STN: 3 Mar 2004
AB
     Cellular localization during development is crucial to the correct
     formation of tissues and organs in all multicellular organisms. The 14
     members of the Eph family of receptor tyrosine kinases and their ligands
     play an important role in establishing and maintaining the correct
     positionings of cells. EphA2 is primarily expressed in
     epithelial cells, where its expression is tightly regulated by
     phosphorylation and degradation. Loss of regulation decreases
     phosphorylation, increases protein concentration, and leads to a
     transformed phenotype resulting in highly aggresive tumors. In order to
     investigate the activity and regulation of EphA2, the
     cytoplasmic domains (kinase and SAM domains) have been cloned into a
     bacterial vector for expression in E. coli. Protein expression has been
     optimized in order to obtain soluble, active protein, and the protein has
     been purified by affinity chromatography. Characterization of the
     expressed protein has determined that the kinase domain is active and the
     protein is purified in a phosphorylated state. Further studies to
     investigate the activity and oligomeric state of the cytoplasmic domains
     will be described.
     General biology - Symposia, transactions and proceedings
                                                                00520
     Biochemistry studies - General
                                      10060
     Biochemistry studies - Proteins, peptides and amino acids
                                                                 10064
     Physiology and biochemistry of bacteria
IT
     Major Concepts
        Biochemistry and Molecular Biophysics; Methods and Techniques
IT
     Chemicals & Biochemicals
          EphA2: characterization, cytoplasmic domains, expression,
        purification, receptor tyrosine kinase; protein: concentration
IT
     Methods & Equipment
        affinity chromatography: chromatographic techniques, laboratory
        techniques; protein characterization: laboratory techniques
ORGN Classifier
        Enterobacteriaceae
                             06702
     Super Taxa
        Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria;
        Microorganisms
     Organism Name
        Escherichia coli (species)
     Taxa Notes
        Bacteria, Eubacteria, Microorganisms
ORGN Classifier
       Hominidae
                    86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
       human (common)
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
L59
    ANSWER 2 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
     2004:86106 BIOSIS
AN
```

```
DN
     PREV200400085138
     CD8+ and CD4+ T cell-mediated immunity against novel EphA2
TI
     -derived epitopes in patients with renal cell carcinoma.
    Herrem, Christopher J. [Reprint Author]; Tatsumi, Tomohide; Olson, Walter;
ΑU
     Finke, James H.; Bukowski, Ronald M.; Kinch, Michael S.;
     Storkus, Walter J.
     Immunology, Medical School, University of Pittsburgh, 5117 Centre Avenue,
CS
     Pittsburgh, PA, 15213, USA
     FASEB Journal, (April 14 2003) Vol. 17, No. 7, pp. C333. print.
SO
    Meeting Info.: 90th Anniversary Annual Meeting of the American
     Association of Immunologists. Denver, CO, USA. May 06-10, 2003.
     American Association of Immunologists.
     ISSN: 0892-6638 (ISSN print).
TG
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
    English
LA
    Entered STN: 11 Feb 2004
ED
    Last Updated on STN: 11 Feb 2004
CC
     General biology - Symposia, transactions and proceedings
     Cytology - Animal 02506
     Cytology - Human
                       02508
     Blood - Blood and lymph studies
     Blood - Blood cell studies
                                  15004
     Urinary system - Pathology
                                  15506
     Neoplasms - Immunology
                             24003
     Neoplasms - Pathology, clinical aspects and systemic effects
                                                                   24004
     Immunology - General and methods
                                       34502
     Immunology - Immunopathology, tissue immunology
                                                       34508
IT
     Major Concepts
        Clinical Immunology (Human Medicine, Medical Sciences); Oncology (Human
       Medicine, Medical Sciences)
     Parts, Structures, & Systems of Organisms
IT
        CD4-positive T cells: blood and lymphatics, immune system, EphA-2
        derived epitope response, renal cell carcinoma, renal cell carcinoma
        study; CD8-positive T cells: blood and lymphatics, immune system,
        EphA-2 derived epitope response, renal cell carcinoma, renal cell
        carcinoma study
IT
    Diseases
        renal cell carcinoma: neoplastic disease, urologic disease, immunology
        Carcinoma, Renal Cell (MeSH); Kidney Neoplasms (MeSH)
TT
     Chemicals & Biochemicals
        EphA-2 derived epitopes: CD4-positive T cell mediated immunity,
        CD8-positive T cell mediated immunity, renal cell carcinoma study
ORGN Classifier
       Hominidae
                    86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
       human (common): patient
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
    ANSWER 3 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
L59
     2003:503134 BIOSIS
AN
     PREV200300498778
DN
     Antibody targeting of the EphA2 receptor tyrosine kinase on
ΤI
     breast cancer cells.
ΑU
     Hu, Min [Reprint Author]; Kinch, Michael S.
     Purdue University, West Lafayette, IN, USA
CS
     Proceedings of the American Association for Cancer Research
SO
```

```
Annual Meeting, (July 2003) Vol. 44, pp. 1234. print.
     Meeting Info.: 94th Annual Meeting of the American Association for
     Cancer Research. Washington, DC, USA. July 11-14, 2003.
     ISSN: 0197-016X.
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LΑ
     English
     Entered STN: 29 Oct 2003
ED
     Last Updated on STN: 29 Oct 2003
CC
     General biology - Symposia, transactions and proceedings
     Enzymes - General and comparative studies: coenzymes 10802
     Reproductive system - Physiology and biochemistry
     Reproductive system - Pathology
                                       16506
     Neoplasms - Immunology 24003
     Neoplasms - Pathology, clinical aspects and systemic effects
                                                                    24004
     Immunology - General and methods 34502
     Immunology - Immunopathology, tissue immunology
                                                       34508
IT
     Major Concepts
        Enzymology (Biochemistry and Molecular Biophysics); Immune System
        (Chemical Coordination and Homeostasis); Tumor Biology
IT
     Parts, Structures, & Systems of Organisms
        breast: reproductive system
IT
     Diseases
        breast cancer: neoplastic disease, reproductive system disease/female
        Breast Neoplasms (MeSH)
IT
     Chemicals & Biochemicals
          EphA2 receptor tyrosine kinase: phosphorylation; monoclonal
        antibody
IT
     Miscellaneous Descriptors
        antibody targeting
ORGN Classifier
       Hominidae
                    86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        MCF-10A cell line (cell line): human breast cancer cells
        MDA-MB-231 cell line (cell line): human breast cancer cells
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN
     149433-91-0 (EphA2 receptor tyrosine kinase)
1.59
     ANSWER 4 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ΔN
     2003:502353 BIOSIS
DN
     PREV200300498371
TI
     Epitope targeting of EphA2: New opportunities for selective
     killing of tumor cells.
ΑIJ
     Kinch, Michael S. [Reprint Author]; Coffman, Karen [Reprint
     Author]; Carles-Kinch, Kelly [Reprint Author]; Donacki, Nanci E. [Reprint
     Author]; Kiener, Peter A. [Reprint Author]; Langermann,
     Solomon [Reprint Author]; Mancini, Marie [Reprint Author]; Tice,
     David [Reprint Author]; Woods, Robert [Reprint Author]
CS
     MedImmune, Inc, Gaithersburg, MD, USA
SO
     Proceedings of the American Association for Cancer Research
     Annual Meeting, (July 2003) Vol. 44, pp. 1118. print.
     Meeting Info.: 94th Annual Meeting of the American Association for
     Cancer Research. Washington, DC, USA. July 11-14, 2003.
     ISSN: 0197-016X.
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LΑ
     English
```

```
ED
     Entered STN: 29 Oct 2003
     Last Updated on STN: 29 Oct 2003
CC
     General biology - Symposia, transactions and proceedings
     Neoplasms - Pathology, clinical aspects and systemic effects
IT
     Major Concepts
        Tumor Biology
IT
     Diseases
        tumor: neoplastic disease
        Neoplasms (MeSH)
     Chemicals & Biochemicals
IT
          EphA2: receptor tyrosine kinase, expression
IT
     Miscellaneous Descriptors
        cell-cell contact; ligand binding; tumor cell growth
ORGN Classifier
                   33000
        Animalia
     Super Taxa
        Animalia
     Organism Name
        animal (common)
     Taxa Notes
        Animals
L59 ANSWER 5 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN
     2003:476294 BIOSIS
DN
     PREV200300476294
ΤI
     Overexpression of EphA2 in urinary bladder cancer.
     Abraham, Shaji [Reprint Author]; Mohammed, Sulma I.; Kanagy, Sarah;
ΑU
     Kinch, Micheal; Knapp, Deborah
CS
     Purdue University, 625 Harrison St, West Lafayette, IN, USA
SO
     Proceedings of the American Association for Cancer Research
     Annual Meeting, (July 2003) Vol. 44, pp. 1070. print.
     Meeting Info.: 94th Annual Meeting of the American Association for
     Cancer Research. Washington, DC, USA. July 11-14, 2003.
     ISSN: 0197-016X.
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LA
     English
ED
     Entered STN: 15 Oct 2003
     Last Updated on STN: 15 Oct 2003
     General biology - Symposia, transactions and proceedings
     Biochemistry studies - Nucleic acids, purines and pyrimidines
     Biochemistry studies - Proteins, peptides and amino acids
                                                                  10064
     Urinary system - Physiology and biochemistry
     Urinary system - Pathology
                                 15506
     Neoplasms - Pathology, clinical aspects and systemic effects
                                                                     24004
IT
     Major Concepts
        Tumor Biology; Urinary System (Chemical Coordination and Homeostasis)
IT
     Diseases
        urinary bladder cancer: neoplastic disease, urologic disease, etiology
        Bladder Neoplasms (MeSH)
IT
     Chemicals & Biochemicals
          EphA2: biomarker, expression; EphA2 mRNA [
        EphA2 messenger RNA]: expression
IT
     Methods & Equipment
        RT-PCR [reverse transcriptase-polymerase chain reaction]: genetic
        techniques, laboratory techniques; immunohistochemistry: immunologic
        techniques, laboratory techniques; western blot analysis: genetic
        techniques, laboratory techniques
ORGN Classifier
        Hominidae
                    86215
```

```
Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        RT4 cell line (cell line): human urinary bladder cancer cells
        TCC-SUP cell line (cell line): human urinary bladder cancer cells
        UMUC-3 cell line (cell line): human urinary bladder cancer cells
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
     ANSWER 6 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
L59
AN
     2003:441702 BIOSIS
DN
     PREV200300441702
TI
     EphA2 expression is associated with aggressive features in
     ovarian carcinoma.
ΑU
     Thaker, Premal H. [Reprint Author]; Kinch, Michael; Sood, Anil
CS
     University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SO
     Proceedings of the American Association for Cancer Research
     Annual Meeting, (July 2003) Vol. 44, pp. 89. print.
     Meeting Info.: 94th Annual Meeting of the American Association for
     Cancer Research. Washington, DC, USA. July 11-14, 2003.
     ISSN: 0197-016X.
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LΑ
     English
     Entered STN: 24 Sep 2003
ED
     Last Updated on STN: 24 Sep 2003
CC
     General biology - Symposia, transactions and proceedings
     Enzymes - General and comparative studies: coenzymes
                                                            10802
     Digestive system - Pathology 14006
     Reproductive system - Physiology and biochemistry
     Reproductive system - Pathology
                                      16506
     Neoplasms - Pathology, clinical aspects and systemic effects
                                                                    24004
IT
     Major Concepts
        Enzymology (Biochemistry and Molecular Biophysics); Reproductive System
        (Reproduction); Tumor Biology
IT
     Diseases
        ascites: digestive system disease
        Ascites (MeSH)
IT
     Diseases
        benign ovarian mass: reproductive system disease/female
ΙT
     Diseases
        ovarian carcinoma: neoplastic disease, reproductive system
        disease/female
        Ovarian Neoplasms (MeSH); Carcinoma (MeSH)
     Chemicals & Biochemicals
IT
        epithelial cell kinase A2 [EphA2]: expression
     Miscellaneous Descriptors
IT
        tumor grade
ORGN Classifier
       Hominidae
                    86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        human (common): middle age, patient, female
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
L59 ANSWER 7 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN
     2003:270640 BIOSIS
```

```
DN
     PREV200300270640
TI
     Ligand (ephrin-A1) binding upregulates EphA2 gene expression.
     Pratt, Rebecca Lynn [Reprint Author]; Kinch, Michael S.
ΑU
CS
     Basic Medical Sciences, Purdue University, 625 Harrison Street, West
     Lafayette, IN, 47907-2026, USA
     rlp@vet.purdue.edu; kinchm@medimmune.com
SO
     FASEB Journal, (March 2003) Vol. 17, No. 4-5, pp. Abstract No.
     146.9. http://www.fasebj.org/. e-file.
     Meeting Info.: FASEB Meeting on Experimental Biology: Translating the
     Genome. San Diego, CA, USA. April 11-15, 2003. FASEB.
     ISSN: 0892-6638 (ISSN print).
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LΑ
     English
ED
     Entered STN: 11 Jun 2003
     Last Updated on STN: 11 Jun 2003
     The EphA2 receptor tyrosine kinase is overexpressed in many
AB
     cancers. Increased levels of EphA2 protein are characteristic
     of a metastatic phenotype because EphA2 overexpression
     positively regulates many different aspects of malignancy, including tumor
     cell growth, migration and invasion. While the relationship between
     EphA2 and these biological outcomes has been the subject of much
     recent investigation, less is known of the mechanisms that govern
     EphA2 gene expression. Our present studies demonstrate that
     EphA2 gene expression is positively regulated by its own ability
     to bind ligand (ephrin-A1). Treatment of malignant (MDA-MB-231) or
     non-transformed (MCF10A) breast epithelial lines with artificial ligands
     induced EphA2 gene expression whereas antagonists of
     EphA2-ligand binding decreased EphA2 mRNA levels. We
     also demonstrate that Ephrin-Al-mediated induction of EphA2 gene
     expression requires intracellular signaling through the MAP/ERK kinase
     pathway. These findings provide intriguing evidence that EphA2
     expression and function are intimately linked in both non-transformed and
     malignant epithelial cells. Ultimately, this information could help to
     understand the mechanisms that cause the increased expression of this
     important and influential oncogene in human cancer.
CC
     General biology - Symposia, transactions and proceedings
     Genetics - General
                          03502
     Genetics - Human
                        03508
     Neoplasms - Pathology, clinical aspects and systemic effects
                                                                    24004
IT
     Major Concepts
        Molecular Genetics (Biochemistry and Molecular Biophysics); Tumor
        Biology
IT
     Diseases
        cancer: neoplastic disease
        Neoplasms (MeSH)
IT
     Diseases
        metastasis: neoplastic disease
IT
     Chemicals & Biochemicals
          EphA2: receptor tyrosine kinase; EphA2 mRNA [
        EphA2 messenger RNA]; ephrin-A1
ΙT
     Miscellaneous Descriptors
        MAP/ERK kinase pathway; tumor cell growth; tumor cell invasion; tumor
        cell migration
ORGN Classifier
        Hominidae
                    86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        MCF10A cell line (cell line): human non-transformed breast epithelial
```

```
cells
        MDA-MB-231 cell line (cell line): human malignant breast epithelial
        cells
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
GEN
     human EphA2 gene (Hominidae): expression, oncogene
L59
     ANSWER 8 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
     2003:82261 BIOSIS
AN
     PREV200300082261
DN
TΙ
     EphA2 overexpression in breast cancer decreases estrogen
     dependence.
     Lu, M. [Reprint Author]; Miller, K. D.; Polar, Y.; Nakshatri, H.;
ΑU
     Kinch, M.
     Purdue University Cancer Center, West Lafayette, IN, USA
CS
so
     Breast Cancer Research and Treatment, (December 2002) Vol. 76, No.
     Supplement 1, pp. S144. print.
     Meeting Info.: 25th Annual San Antonio Breast Cancer Symposium.
     San Antonio, TX, USA. December 11-14, 2002.
     ISSN: 0167-6806 (ISSN print).
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
       Conference; (Meeting Poster)
LA
     English
ED
     Entered STN: 6 Feb 2003
     Last Updated on STN: 6 Feb 2003
     General biology - Symposia, transactions and proceedings
                                                                00520
     Biochemistry studies - General 10060
     Biochemistry studies - Proteins, peptides and amino acids
                                                                 10064
     Reproductive system - Physiology and biochemistry
     Reproductive system - Pathology
                                      16506
     Neoplasms - Pathology, clinical aspects and systemic effects
                                                                     24004
IT
     Major Concepts
        Biochemistry and Molecular Biophysics; Reproductive System
        (Reproduction); Tumor Biology
IT
     Diseases
        breast cancer: neoplastic disease, reproductive system disease/female
        Breast Neoplasms (MeSH)
IT
     Chemicals & Biochemicals
          EphA2: overexpression, receptor tyrosine kinase; estrogen;
        estrogen receptor
     Miscellaneous Descriptors
IT
        estrogen dependence
ORGN Classifier
       Hominidae
                    86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
       MCF-7 cell line (cell line)
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
L59 ANSWER 9 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN
     2002:511226 BIOSIS
DN
     PREV200200511226
TI
     Design and synthesis of tyrosine phosphatase inhibitor directed toward new
     cancer treatments.
AU
     Zabell, Adam P. R. [Reprint author]; Stauffacher, Cynthia [Reprint
```

author]; Kinch, Michael [Reprint author]; Katsuyama, Isamu;

Wiest, Olaf; Helquist, Paul

```
CS
     Walther Cancer Institute, Purdue University, West Lafayette, IN, 47907,
     USA
     ikatsuya@nd.edu
SO
     Abstracts of Papers American Chemical Society, (2002) Vol. 224,
     No. 1-2, pp. ORGN 130. print.
     Meeting Info.: 224th National Meeting of the American Chemical
     Society. Boston, MA, USA. August 18-22, 2002.
     CODEN: ACSRAL. ISSN: 0065-7727.
DΤ
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LΑ
     English
     Entered STN: 2 Oct 2002
ED
     Last Updated on STN: 2 Oct 2002
CC
     General biology - Symposia, transactions and proceedings
                                                                  00520
     Pathology - Therapy 12512
     Pharmacology - General
                               22002
     Neoplasms - Pathology, clinical aspects and systemic effects
                                                                      24004
     Neoplasms - Therapeutic agents and therapy
IT
     Major Concepts
        Pharmacology
IT
     Diseases
        cancer: neoplastic disease
        Neoplasms (MeSH)
IT
     Chemicals & Biochemicals
          EphA2; HCPTP; tyrosine phosphatase inhibitor:
        antineoplastic-drug, enzyme inhibitor-drug
IT
     Methods & Equipment
        computational design: analytical method
IT
     Miscellaneous Descriptors
        drug development; metastasis; Meeting Abstract
     ANSWER 10 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
L59
     2002:409529 BIOSIS
AN
     PREV200200409529
DN
TI
     Molecular regulation of melanoma tumor cell vasculogenic mimicry by
     EphA2 and VE-cadherin: A novel signaling pathway.
ΑU
     Hess, Angela R. [Reprint author]; Seftor, Elisabeth A.; Gruman, Lynn M.;
     Kinch, Michael S.; Seftor, Richard E. B.; Hendrix, Mary J. C.
CS
     University of Iowa, Iowa City, IA, USA
SO
     Proceedings of the American Association for Cancer Research
     Annual Meeting, (March, 2002) Vol. 43, pp. 843. print.
     Meeting Info.: 93rd Annual Meeting of the American Association for
     Cancer Research. San Francisco, California, USA. April 06-10, 2002.
     ISSN: 0197-016X.
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LA
     English
     Entered STN: 31 Jul 2002
ED
     Last Updated on STN: 23 Sep 2002
CC
     General biology - Symposia, transactions and proceedings
     Enzymes - General and comparative studies: coenzymes
     Cardiovascular system - Physiology and biochemistry Integumentary system - Physiology and biochemistry
     Integumentary system - Pathology 18506
     Neoplasms - Pathology, clinical aspects and systemic effects
IT
     Major Concepts
        Cardiovascular System (Transport and Circulation); Enzymology
        (Biochemistry and Molecular Biophysics); Integumentary System (Chemical
        Coordination and Homeostasis); Tumor Biology
```

```
IT
     Parts, Structures, & Systems of Organisms
        skin: integumentary system; vascular endothelium: circulatory system
IT
        melanoma: integumentary system disease, neoplastic disease
        Melanoma (MeSH)
IT
     Chemicals & Biochemicals
          EphA2: expression; FRNK: expression; LY294002: enzyme
        inhibitor-drug; VE-cadherin [vascular endothelium-cadherin]:
        expression; focal adhesion kinase [FAK]: phosphorylation;
        phosphoinositide 3-kinase [PI3K]
IT
     Miscellaneous Descriptors
        tumor cell vasculogenic mimicry regulation; Meeting Abstract
ORGN Classifier
        Animalia
                   33000
     Super Taxa
        Animalia
     Organism Name
        animal
     Taxa Notes
        Animals
     154447-36-6 (LY294002)
RN
     144114-16-9 (focal adhesion kinase)
     144114-16-9 (FAK)
     115926-52-8 (PHOSPHOINOSITIDE 3-KINASE)
L59 ANSWER 11 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
AN
     2002:396016 BIOSIS
DN
     PREV200200396016
TI
     Stimulation of the oncoprotein, EphA2, activates the ERK
     signaling pathway: Linking the biochemical and biological consequences of
     ligand binding.
ΑU
     Pratt, Rebecca L. [Reprint author]; Kinch, Michael S. [Reprint
     authorl
CS
     Purdue University, West Lafayette, IN, USA
SO
     Proceedings of the American Association for Cancer Research
     Annual Meeting, (March, 2002) Vol. 43, pp. 726. print.
     Meeting Info.: 93rd Annual Meeting of the American Association for
     Cancer Research. San Francisco, California, USA. April 06-10, 2002.
     ISSN: 0197-016X.
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LA
     English
     Entered STN: 24 Jul 2002
ED
     Last Updated on STN: 24 Jul 2002
CC
     General biology - Symposia, transactions and proceedings
     Enzymes - General and comparative studies: coenzymes
IT
     Major Concepts
        Enzymology (Biochemistry and Molecular Biophysics)
ΙT
     Chemicals & Biochemicals
        ERK [extracellular signal-regulated kinase]: phosphorylation,
        regulation, signaling; Elk-1: transcription factor; Eph2: expression,
        oncoprotein; GRB2: adaptor protein; SHC: adaptor protein
     Miscellaneous Descriptors
IT
        ligand binding; Meeting Abstract
RN
     142243-02-5 (EXTRACELLULAR SIGNAL-REGULATED KINASE)
    ANSWER 12 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
L59
     STN
ΆN
     2002:22133 BIOSIS
```

```
DN
     PREV200200022133
ΤI
     The mechanism of EphA2 protein degradation: Implications of
     increased EphA2 protein levels in metastatic cancer cells.
     Walker-Daniels, Jennifer L. [Reprint author]; Van Horn, Deborah A.
AU
     [Reprint author]; Kinch, Michael S. [Reprint author]
CS
     Purdue University, West Lafayette, IN, USA
     Proceedings of the American Association for Cancer Research
SO
     Annual Meeting, (March, 2001) Vol. 42, pp. 840. print.
     Meeting Info.: 92nd Annual Meeting of the American Association for
     Cancer Research. New Orleans, LA, USA. March 24-28, 2001.
     ISSN: 0197-016X.
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LA
     English
ED
     Entered STN: 26 Dec 2001
     Last Updated on STN: 25 Feb 2002
CC
     General biology - Symposia, transactions and proceedings
     Neoplasms - Pathology, clinical aspects and systemic effects
IT
     Major Concepts
        Tumor Biology
     Diseases
IT
        metastatic cancer: neoplastic disease
        Neoplasm Metastasis (MeSH)
IT
     Chemicals & Biochemicals
        EphA-2 protein: increased metastatic tumor cell level implications,
        metastatic tumor cell degradation mechanism
IT
     Miscellaneous Descriptors
          Meeting Abstract
ORGN Classifier
        Animalia
                   33000
     Super Taxa
        Animalia
     Organism Name
        animal: animal model
     Taxa Notes
        Animals
    ANSWER 13 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
L59
     2001:244422 BIOSIS
ΑN
DN
     PREV200100244422
     EphA2 overexpression alters cellular adhesions: Implications for
ΤI
     metastasis.
     Zelinski, Daniel Paul [Reprint author]; Kinch, Michael [Reprint
AU
     authorl
     Purdue University, 1322 Lynn Hall, West Lafayette, IN, 47906, USA
CS
SO
     FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A234. print.
    Meeting Info.: Annual Meeting of the Federation of American Societies
     for Experimental Biology on Experimental Biology 2001. Orlando,
     Florida, USA. March 31-April 04, 2001.
     CODEN: FAJOEC. ISSN: 0892-6638.
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LΑ
    English
ED
    Entered STN: 23 May 2001
    Last Updated on STN: 19 Feb 2002
    Many of the most deadly forms of cancer arise when a population of tumor
     cells gains the ability to survive and grow in a foreign microenvironment.
    At the cellular level, metastasis requires alterations in cellular
     adhesions that permit detachment from the primary tumor and invasion
```

through the underlying basement membrane. However, the causes for these changes in adhesion are poorly understood. Studies in our laboratory have linked these changes with the EphA2 (Eck) receptor tyrosine kinase, which is overexpressed in many metastatic cancers. To study the effects of EphA2 on cancer progression and pathogenesis, we overexpressed EphA2 in a non-transformed breast epithelial cell line, MCF-10A1. In vitro assays for transformation showed that EphA2 overexpression is sufficient to promote invasiveness and anchorage independent growth. EphA2-overexpressing cells demonstrated tumorigenic and metastatic potential in xenograft studies. During our assessment of these cells, we noted dramatic changes in their cellular morphology that resembled metastatic cells. Objective measurements of cellular adhesions revealed that the EphA2-overexpressing cells had decreased cell-cell adhesions and increased cell-ECM adhesions. Our analyses have demonstrated a change in ECM substrate preferences that implicates a change in integrin expression. We are currently investigating the mechanisms by which EphA2 overexpression changes the adhesive behavior of epithelial cells, which is important because this information will provide critical insight into the fundamental causes of metastasis. Biochemistry studies - General General biology - Symposia, transactions and proceedings 00520 Cytology - General 02502 Cytology - Animal 02506 Neoplasms - Pathology, clinical aspects and systemic effects 24004 Major Concepts Biochemistry and Molecular Biophysics; Cell Biology; Tumor Biology Parts, Structures, & Systems of Organisms epithelial cells, adhesive behavior; extracellular matrix Chemicals & Biochemicals EphA2 protein: expression Miscellaneous Descriptors cellular adhesion: alteration; metastasis; Meeting Abstract ANSWER 14 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on L59 STN 2000:238522 BIOSIS PREV200000238522 EphA2 overexpression in breast cancer: Regulation by estrogen and c-Myc. Zelinski, Daniel P. [Reprint author]; Dodge-Zantek, Nicole [Reprint author]; Stewart, Jane C. [Reprint author]; Peters, Mette A. [Reprint author]; Taparowsky, Elizabeth J. [Reprint author]; Kinch, Michael S. [Reprint author] Purdue Univ, West Lafayette, IN, USA Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 358. print. Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 01-05, 2000. ISSN: 0197-016X. Conference; (Meeting) Conference; Abstract; (Meeting Abstract) English Entered STN: 7 Jun 2000 Last Updated on STN: 5 Jan 2002 Neoplasms - General 24002 Biophysics - Membrane phenomena 10508

CC

IT

IT

IT

IT

AN

DN ΤI

ΑU

CS

SO

 \mathtt{DT}

LΑ

ED

CC

Reproductive system - Pathology

Endocrine - Gonads and placenta

16506

17006

General biology - Symposia, transactions and proceedings 00520 Biochemistry studies - Sterols and steroids IT Major Concepts Reproductive System (Reproduction); Tumor Biology IT breast cancer: neoplastic disease, reproductive system disease/female Breast Neoplasms (MeSH) Chemicals & Biochemicals IT EphA2 receptor; c-Myc; estrogen ΙT Miscellaneous Descriptors cancer progression; Meeting Abstract L59 ANSWER 15 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN AN 2000:82525 BIOSIS DN PREV200000082525 ΤI Overexpression of EphA2 in metastatic cancer cells: A role for Ras signaling. AU Walker-Daniels, Jennifer L. [Reprint author]; Zantek, Nicole D. [Reprint author]; Azimi, Minou [Reprint author]; Kinch, Michael S. [Reprint author] CS Purdue University, 1246 Lynn Hall, West Lafayette, IN, 47907-1246, USA Molecular Biology of the Cell, (Nov., 1999) Vol. 10, No. SUPPL., pp. 427a. SO print. Meeting Info.: 39th Annual Meeting of the American Society for Cell Biology. Washington, D.C., USA. December 11-15, 1999. The American Society for Cell Biology. CODEN: MBCEEV. ISSN: 1059-1524. DT Conference; (Meeting) Conference; Abstract; (Meeting Abstract) English T.A Entered STN: 1 Mar 2000 ED Last Updated on STN: 3 Jan 2002 CC Neoplasms - General 24002 Cytology - General 02502 Biochemistry studies - General 10060 Metabolism - General metabolism and metabolic pathways 13002 Reproductive system - General and methods Urinary system - General and methods 15501 General biology - Symposia, transactions and proceedings 00520 IT Major Concepts Biochemistry and Molecular Biophysics; Tumor Biology IT Parts, Structures, & Systems of Organisms metastatic cancer cells IT Diseases breast cancer: neoplastic disease, reproductive system disease/female Breast Neoplasms (MeSH) IT Diseases epithelial cancers: neoplastic disease IT Diseases prostate cancer: neoplastic disease, reproductive system disease/male, urologic disease Prostatic Neoplasms (MeSH) TT Chemicals & Biochemicals EphA2: overexpression; Ras IT Miscellaneous Descriptors Meeting Abstract

L59 ANSWER 16 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

```
AN
     1999:187448 BIOSIS
DN
     PREV199900187448
TI
     Regulation of the EphA2 receptor tyrosine kinase by estrogen and
ΑU
     Zantek, N. D.; Zelinski, D.; Peters, M. A.; Taparowsky, E. J.; Kinch,
     M. S.
CS
     Purdue Univ., West Lafayette, IN 47907, USA
so
     Proceedings of the American Association for Cancer Research
     Annual Meeting, (March, 1999) Vol. 40, pp. 687. print.
     Meeting Info.: 90th Annual Meeting of the American Association for
     Cancer Research. Philadelphia, Pennsylvania, USA. April 10-14, 1999.
     American Association for Cancer Research.
     ISSN: 0197-016X.
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
LA
     English
     Entered STN: 5 May 1999
ED
     Last Updated on STN: 5 May 1999
CC
     Enzymes - General and comparative studies: coenzymes
                                                             10802
     Biochemistry studies - General
                                      10060
     Reproductive system - General and methods
                                                  16501
     Neoplasms - General
                           24002
       General biology - Symposia, transactions and proceedings
                                                                   00520
IT
     Major Concepts
        Enzymology (Biochemistry and Molecular Biophysics); Tumor Biology
IT
     Diseases
        breast cancer: neoplastic disease, reproductive system disease/female
        Breast Neoplasms (MeSH)
IT
     Chemicals & Biochemicals
        c-myc protein: transcription factor; estrogen; EphA2 receptor
        tyrosine kinase: regulation
IT
     Miscellaneous Descriptors
          Meeting Abstract
RN
     149433-91-0 (EphA2 receptor tyrosine kinase)
     80449-02-1 (TYROSINE KINASE)
L59
    ANSWER 17 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
     STN
AN
     1999:26830 BIOSIS
DN
     PREV199900026830
ΤI
     Epithelial cell kinase (ECK/EPHA2) regulation in breast cancer.
AU
     Zantek, Nicole Dodge [Reprint author]; Fedor-Chaiken, Mary; Brackenbury,
     Robert; Kinch, Michael S.
     Dep. Basic Med. Sci., Purdue Univ., West Lafayette, IN 47907, USA
CS
     Molecular Biology of the Cell, (Nov., 1998) Vol. 9, No. SUPPL., pp. 134A.
SO
     print.
     Meeting Info.: 38th Annual Meeting of the American Society for Cell
     Biology. San Francisco, California, USA. December 12-16, 1998.
     American Society for Cell Biology.
     CODEN: MBCEEV. ISSN: 1059-1524.
DT
     Conference; (Meeting)
       Conference; Abstract; (Meeting Abstract)
T.A
     English
     Entered STN: 20 Jan 1999
ED
     Last Updated on STN: 20 Jan 1999
CC
     Neoplasms - General
                           24002
     Cytology - General
                          02502
     Biochemistry studies - General
                                      10060
     Enzymes - General and comparative studies: coenzymes
                                                             10802
     Reproductive system - General and methods
```

```
General biology - Symposia, transactions and proceedings
                                                                    00520
IT
     Major Concepts
        Enzymology (Biochemistry and Molecular Biophysics); Tumor Biology
IT
     Diseases
        breast cancer: neoplastic disease, reproductive system disease/female
        Breast Neoplasms (MeSH)
IT
     Chemicals & Biochemicals
        E-cadherin; Epithelial Cell Kinase [ECK/EphA2]: Eph family
        tyrosine kinase, breast cancer progression marker
TΤ
     Miscellaneous Descriptors
          Meeting Abstract
     9031-44-1 (KINASE)
RN
     80449-02-1 (TYROSINE KINASE)
=> d his
     (FILE 'HOME' ENTERED AT 11:26:38 ON 07 JUL 2005)
                SET COST OFF
     FILE 'HCAPLUS' ENTERED AT 11:26:44 ON 07 JUL 2005
                E EPH
L1
              4 S E3()A2
L2
            154 S E29,E32
L3
            156 S L1, L2
                E KIENER P/AU
L4
             99 S E3, E4, E7, E8
                E KINCH M/AU
L5
             66 S E3, E5, E7, E10, E11
                E LANGERMAN S/AU
L6
             37 S E4, E5, E11-E14
                E MEDIMMUN/PA,CS
L7
            218 S MEDIMMUNE?/PA,CS
              1 S US20050049176/PN OR (US2004-823259# OR WO2004-US11481 OR US20
L8
L9
              1 S L3 AND L8
            106 S L3 AND (PD<=20030411 OR PRD<=20030411 OR AD<=20030411)
L10
L11
             59 S EPHRIN TYPE A RECEPTOR 2
L12
             27 S L11 AND (PD<=20030411 OR PRD<=20030411 OR AD<=20030411)
L13
            117 S L10,L12
     FILE 'REGISTRY' ENTERED AT 11:33:54 ON 07 JUL 2005
                E EPH/CN
                E EPHA2
             27 S E3
L14
L15
              0 S EPH A2
     FILE 'HCAPLUS' ENTERED AT 11:36:36 ON 07 JUL 2005
L16
            130 S L14
L17
             25 S ECK() (KINASE OR RECEPTOR KINASE OR RECEPTOR PROTEIN KINASE OR
L18
              1 S EPITHELIAL CELL RECEPTOR PROTEIN TYROSINE KINASE
L19
            117 S L16-L18 AND (PD<=20030411 OR PRD<=20030411 OR AD<=20030411)
            174 S L13, L19
L20
             29 S L4-L7 AND L20
L21
L22
             29 S L21 AND (?KINASE? OR TYROSINE OR PROTEINKINASE OR PROTEIN KIN
L23
             28 S L22 AND RECEPTOR
L24
             29 S L22, L23
L25
             29 S L9, L24
L26
             14 S L4-L7 AND L3, L11, L16-L18 NOT L25
            193 S L3,L11,L16-L18 NOT L25,L26
L27
L28
            145 S L27 AND L10, L12, L19
```

```
9 S L28 AND ANTAGON?
L29
L30
            61 S L28 AND (INHIBIT? OR BLOCK? OR PREVENT?)
L31
             62 S L29, L30
                SEL DN AN 3 6 14-16 20 30 34 39 47 48 50 52 53 60
L32
             15 S L31 AND E1-E45
L33
             44 S L25, L32
L34
             83 S L28 NOT L31, L25, L26
                SEL DN AN 4 5 8 26 27 32 34 38 41 68 83
L35
             11 S L34 AND E46-E78
L36
             55 S L33, L35 AND L1-L13, L16-L35
             55 S L36 AND (?TYROSIN? OR ?KINASE? OR RECEPTOR OR PROTEIN)
L37
L38
             10 S L37 AND ECK
             51 S L37 AND (EPH OR EPHRIN? OR EPH## OR EPH A#)
L39
             55 S L37-L39
L40
                SEL HIT RN
     FILE 'REGISTRY' ENTERED AT 12:19:56 ON 07 JUL 2005
L41
              2 S E79-E80
L42
              2 S L41 AND L14
     FILE 'REGISTRY' ENTERED AT 12:20:37 ON 07 JUL 2005
     FILE 'HCAPLUS' ENTERED AT 12:20:44 ON 07 JUL 2005
     FILE 'MEDLINE' ENTERED AT 12:22:57 ON 07 JUL 2005
L43
              0 S L14
            116 S L17 OR L18 OR L1 OR L2 OR L11
L44
                E EPH
L45
              3 S E3()A2
L46
            111 S E18
L47
             86 S L44-L46 AND PY<=2003
              3 S L47 NOT AB/FA
L48
                SEL DN AN 1
L49
              1 S E1-E2 AND L48
L50
             83 S L47 NOT L48
                SEL DN AN L50 2 13 16 17 19 20 22 32 34 69
L51
             10 S L50 AND E3-E22
L52
             11 S L49, L51
     FILE 'MEDLINE' ENTERED AT 12:31:34 ON 07 JUL 2005
     FILE 'BIOSIS' ENTERED AT 12:31:45 ON 07 JUL 2005
                E KIENERP/AU
                E KIENER/AU
            108 S E23-E26
L53
                E KINCH M/AU
             68 S E3, E5-E9
L54
                E LANGERMA S/AU
             45 S E18, E22-E24
L55
             11 S L14
L56
            133 S L44
L57
             36 S L53-L55 AND L56,L57
L58
             17 S L58 AND (00520/CC OR (CONFERENCE? OR CONGRESS? OR POSTER? OR
L59
```

=>

FILE 'BIOSIS' ENTERED AT 12:35:37 ON 07 JUL 2005